A STUDY OF SERUM BILIRUBIN IN CORONARY ARTERY DISEASE PATIENTS

SUBMITTED FOR THE MD GENERAL MEDICINE EXAMINATION APRIL 2013 TO THE MGR MEDICAL UNIVERSITY, CHENNAIIN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF MD DEGREE BRANCH I (GENERAL MEDICINE).

CONDUCTED BY

DR.B.PRIYA

BONAFIDE CERTIFICATE

This is to certify that the Thesis- "**A STUDY OF SERUMBILIRUBIN IN CORONARY ARTERY DISEASE PATIENTS"**is a genuine work done by Dr.B.PRIYA, Post-graduate student in Department of Medicine, Government medical college, Kilpauk, under the guidance of Prof.Dr.N.GUNASEKARAN, M.D., DTCD, Head of the Department of Medicine. Kilpauk Medical College.

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DECLARATION

I, **Dr.B.PRIYA**, solemnly declare that the dissertation titled**A STUDY OF SERUM BILIRUBIN IN CORONARY ARTERY DISEASE PATIENTS**has been prepared by me. This is submitted to the Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfilment of the requirement for the award of MD degree Branch I (General Medicine).

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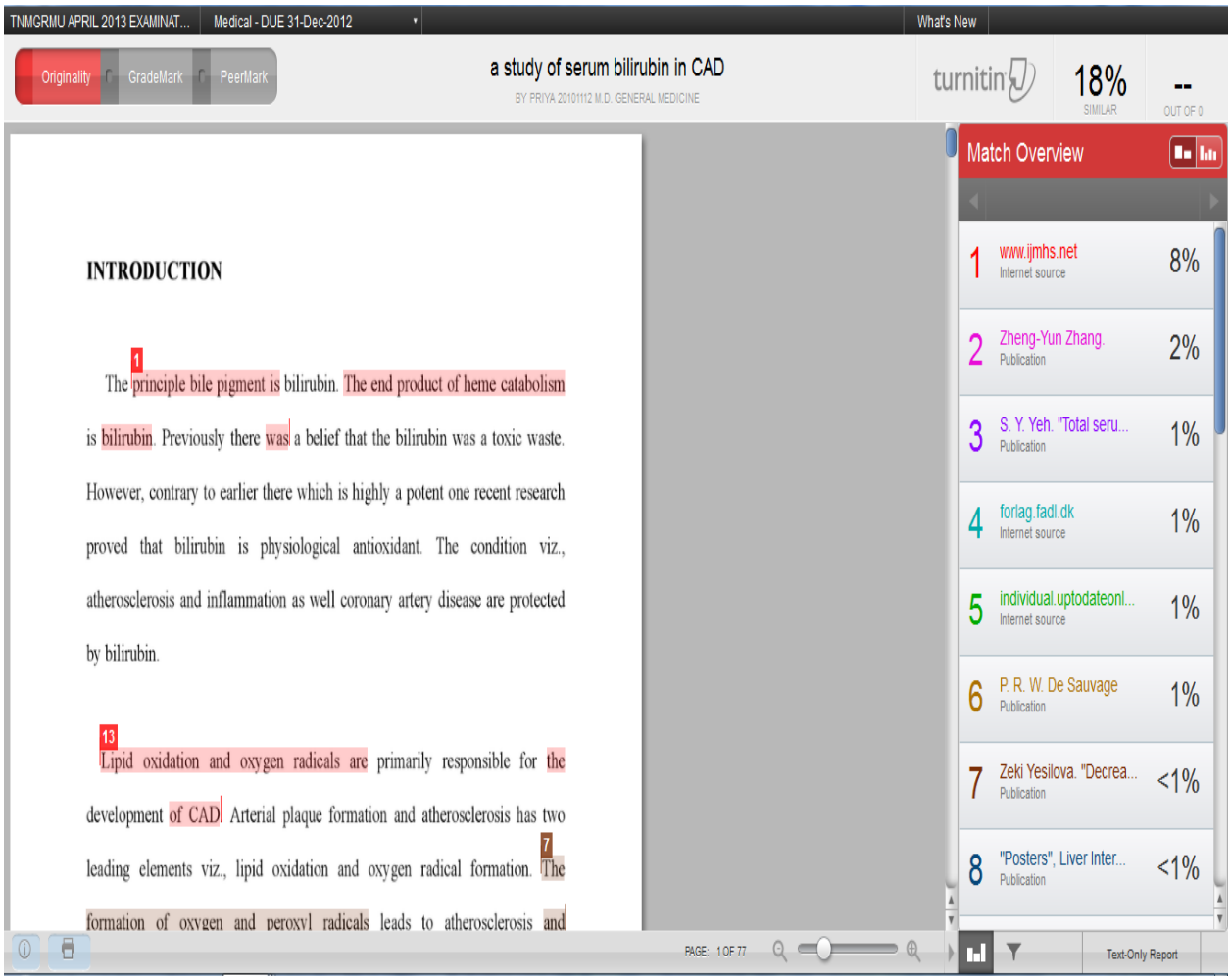
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INTRODUCTION
The principle bile pigment is bilirubin. The end product of heme catabolism is bilirubin. Previously there was a belief that the bilirubin was a toxic waste. However, contrary to earlier there which is highly a potent one recent research proved that bilirubin is physiological antioxidant. The condition viz., atherosclerosis and inflammation as well coronary artery disease are protected by bilirubin.
Lipid oxidation and oxygen radicals are primarily responsible for the development of CAD. Arterial plaque formation and atherosclerosis has two leading elements viz., lipid oxidation and oxygen radical formation. The formation of oxygen and peroxyl radicals leads to atherosclerosis and
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INTRODUCTION

The principle bile pigment is bilirubin. The end product of heme catabolism is bilirubin.Previously there was a belief that the bilirubin was a toxic waste.However, contrary to earlier there which is highly a potent one recent research proved that bilirubin is physiological antioxidant.Atherosclerosis and inflammation as well coronary artery disease are protected by bilirubin.

Lipid oxidation and oxygen radicals are primarily responsible for the development of Coronary Artery Disease. Arterial plaque formation and atherosclerosis have two leading elements viz., lipid oxidation and oxygen radical formation. Theformation of oxygen and peroxyl radicals leads to atherosclerosis and inflammation.

It is widely known that bilirubin has antioxidant properties. It has role to protect the atherosclerotic process by preventing oxidized LDL formation. Bilirubinis capable of providing potent scavenging effect of peroxyl radicals. Such capability arises out of increase in the circulatory bilirubin.

The circulatory bilirubin plays a physiologic role to protect against the diseases where oxygen and peroxyl radicals are involved.Smoking, blood cholesterol and hypertension are leading risks that contribute for the ischemic heart disease.

The Antioxidants havedietary as well as endogenous protective characteristics.Therefore, more the serumbilirubin concentration higher the prevention of LDL oxidation, eventually the risk of ischemic heart disease is reduced[1-3]. The primary objective of this study dissertation is to test the hypothesis low serum bilirubin is a risk factor for ischemic heart disease. Besides, the dissertation identifies the association of serum bilirubin with multiple variables like age, sex, family history of coronary artery disease, smoking, hypertension, diabetes mellitus and lipid profile.

REVIEW OF LITERATURE

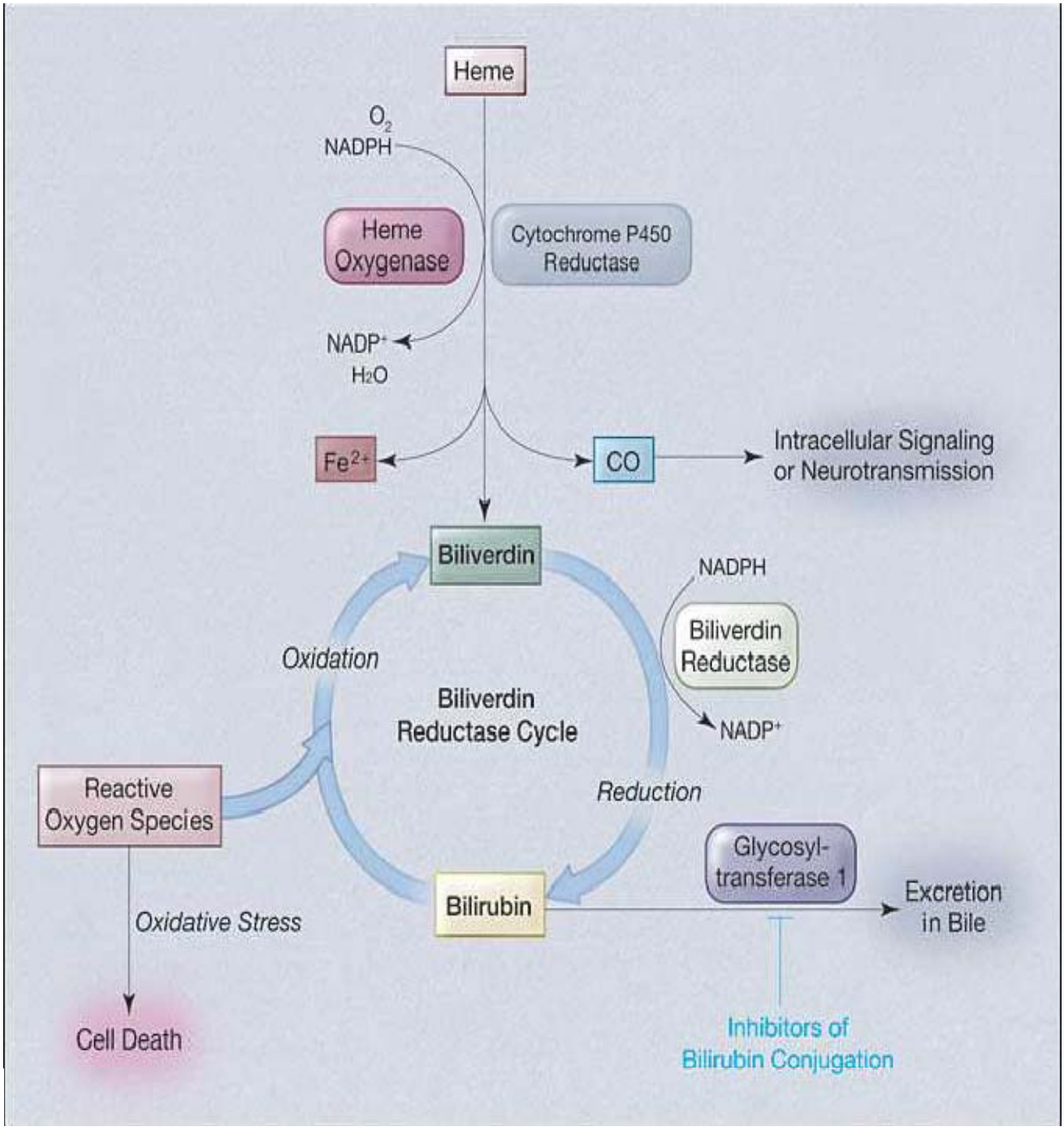
FORMATION OF BILIRUBIN:

The breakdown of heme present in hemoglobin,myoglobin, cytochromes, catalase, peroxidase and tryptophan pyrrolase led to the formation of bilirubin. Hemoglobin yields 80% of the daily bilirubin production (250 to 400 mg in adults). The remaining 20% of serum bilirubin are from hemoproteins and small poolof freehemewhich rapidly turnover. Conditionsassociated with increased red cell turnover such as intravascular or intramedullary hemolysis (eg, megaloblastic, hemolyticand dyserythropoietic anemia's) results in enhanced bilirubin formation.

Afour pyrrole ring connected by carbon bridges anda central ironatom (ferroprotoporphyrin IX) constitutes heme. The catalytic degradation of hemegenerates bilirubin. This sequential reaction is mediated by two groups of enzymes: viz.,

1) Hemeoxygenase

2) Biliverdinreductase


Heme
O_2
NADPH
Heme Oxygenase
Cytochrome P450 Reductase
$NADP^+$
H_2O
Fe^{2+}
CO
Intracellular Signaling or Neurotransmission
Biliverdin
NADPH
Biliverdin Reductase
$NADP^+$
Oxidation
Biliverdin Reductase Cycle
Reduction
Reactive Oxygen Species
Oxidative Stress
Cell Death
Bilirubin
Glycosyl-transferase 1
Excretion in Bile
Inhibitors of Bilirubin Conjugation

Every haem molecule will produce one molecule of bilirubin. These molecules are found in haemoglobin and myoglobin. Also, cytochrome enzymes will also produce one molecule of bilirubin.

The production of bilirubin from haem occurs mainly in the spleen (macrophages) and liver (Kupfer cells), but also all over the body by macrophages, and in renal tubular cells. Bilirubin-forming molecules (i.e. haem) are taken up by reticuloendothelial cells. Inside these cells, Haemoxygenase enzymes break down the haem, removing iron (which is recycled) and carbon monoxide, leaving biliverdin.

Biliverdin is very water soluble, whilst bilirubin is not.Biliverdin is then converted to bilirubin, whilst still in the reticuloendothelial cell. This is done by the enzyme biliverdinreductase.Bilirubin is not just a waste product. It takes up free radicals, and thus is an antioxidant. This is perhaps the benefit of not directly secreting biliverdin, but converting it to bilirubin first.

After bilirubin is released from reticuloendothelial cells, it travels in the blood, bound to albumin. This ensures no bilirubin is excreted in the urine. At very high concentrations, bilirubin can slowly diffuse into the peripheral tissues where it is

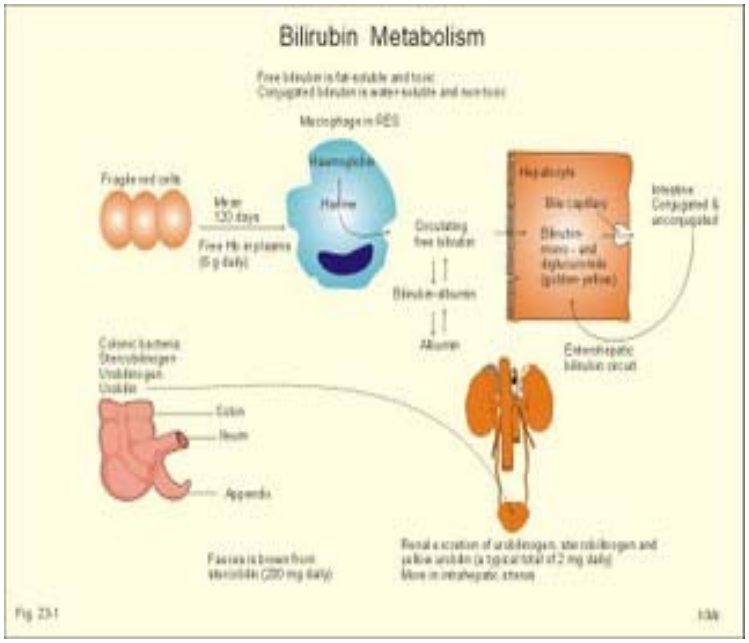
toxic.Bilirubin is then removed from circulation in the sinusoids by hepatocytes. This is a passive process, which occurs down a concentration gradient. The fact that hepatocytes are in direct contact with the sinusoidal fluid helps this process.As soon as bilirubin enters the hepatocyte, it will become bound to glucuronyltransferase which conjugates the bilirubin ready for excretion. Bilirubin is joined with glucuronic acid in the conjugation process. Very small amounts of bilirubin will somehow evade this process and end up in bile as unconjugated bilirubin.

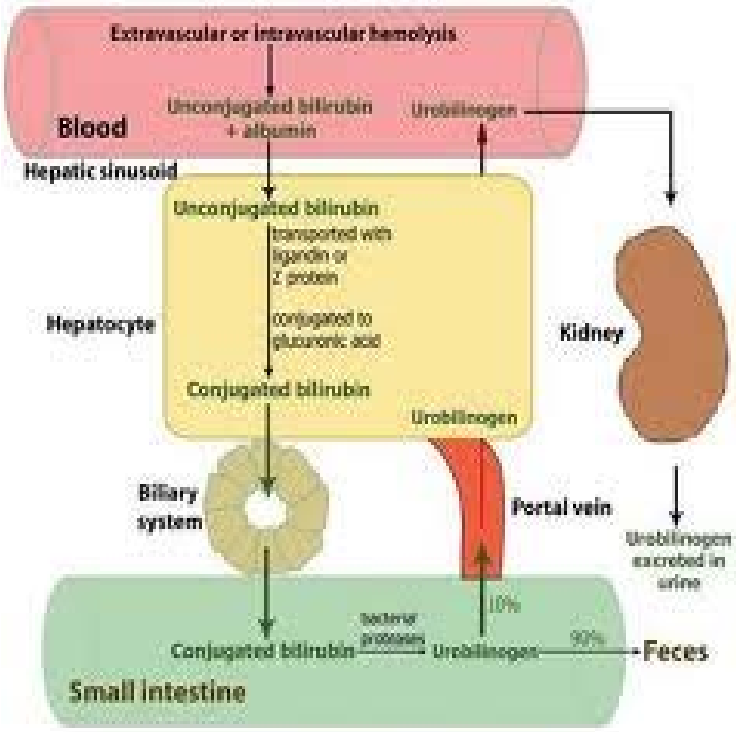
Conjugated bilirubin (bilirubin di- and mono-glucuronide) has the property of water solublity,.so does conjucated bilirubin easily diffuses through the cytoplasm afterwards secreted into the bile canaliculi by an active process. From here conjugated bilirubin is excreted with the bile into the intestine. Bacterial enzymes which arepresent in the colon & terminal ileum hydrolyse the large molecule. The free bilirubin is then reduced to urobilinogen.

Some part of the bilirubin is broken down to substances which is colourless.Hepatocytes produce urobilinogen& by the action of colonic bacteria

results in stercobilinogen. These substancesare oxidised later to yellow coloured urinary urobilin and brown coloured stercobilin excreted via fecaes.

Most of the urobilinogen is excreted in the faeces; the remainder is absorbed in the terminal ileum, returned to the liver via enterohepatic blood, and again excreted into theintestine asbile. A small amount of the urobilinogen is excreted in the normal urine.In situations where the liver cannot excrete conjugated bilirubin, the kidneys will take over this job, however once plasma concentrations are high enough (above 600µmol/L) – the kidneys cannot conjugate bilirubin – only excrete if after this process has occurred. Bilirubin that is deconjugated by bacteria in the gut will be reabsorbed in the colon.





Antioxidant role of Bilirubin:

Multiple studies have shown that different circulating forms of bilirubin are powerful antioxidants, viz. free bilirubin, albumin-bound bilirubin, unconjugated bilirubin and conjugated bilirubin.These forms of bilirubin are effective scavengers of peroxyl radicals .Besides they are able to protect human LDL (low density lipoprotein) against peroxidation[4-8].

The increased physiological concentrations of plasma bilirubin reduces the risk of atherogenesis.The reasons being

a) Involvement of oxidized LDL in the formation of atherogenic plaques

b)Under physiological conditions the abilityof bilirubin to serve as a potent lipid chain-breaking antioxidant[9-10].

It is a established fact that bilirubin is a physiological antioxidant.This fact has been established over the years of experiments in humans and animals.

Yamaguchi and others found that the oxidative metabolites of bilirubin (biotripyrrins) from the urine of healthy human's[11].And also they isolated the metabolites of bilirubin from ascorbic acid-deprived rats treated with endotoxin[12]. Feeding of ascorbic acid resulted in the reduction of bilirubin metabolites which is a physiological antioxidant.It also reduced the hepatic concentration of HO (hemeoxygenase) mRNA principally stimulated by endotoxins.

Multiple studies shows that lower bilirubin concentration results in higher incidence of coronary artery disease,vice versa higher bilirubin subjects had lower occurrence of coronary artery disease[13].

It has also been established that below normal serum bilirubin level is associated with the presence of ischemic heart disease.Schwertner HA and Hopkins PN found that patients with early familial CAD have an average total serum bilirubin of 8.9 ± 6.1 μmol/L and the average level in healthy control subjects is 12.4 ± 8.1 μmol/Lwhich is significantly higher than coronary artery disease patients[14].

Briemer and others observed that cardiovascular risk and bilirubin level have U-shaped relationship.Because of the existence of such relationship they firmly concluded that low concentrations of serum bilirubin are associated with increased risk of ischemic heart disease[15].

Schwertner and MadhavanM on prolonged investigations found that multiple risk factors of CAD is inversely correlate with plasma bilirubin concentration. These risk factors are vizsmoking, LDL-cholesterol, obesity anddiabetes. They further found that the protective factors like HDL-cholesterol, lower FEV1, and lower serum albumin are directly correlating with serum bilirubin[16,17].

On the basis of abovefindings, low bilirubin was found to be an independent risk factor for CAD. Between CAD morbidity and bilirubin concentration an inverse correlation was demonstrated.Hunt[18,19]and others work is an another testimony of the existence of this inverse relationship .They propounded a genetic variation in bilirubin concentration in individuals with early CAD displaying lower bilirubin than unaffected persons.

Circulating bilirubin possesses cardioprotective capacity which in turn associated with reduced risk for CAD. It would be interesting to determine which form of circulating bilirubin is involved in this cardioprotective activity.

Antioxidant activity attributable to any form of bilirubin same is the case with cardioprotective potential of bilibrubin.The known forms are free unconjugated bilirubin, protein-bound unconjugated bilirubin, delta bilirubin, or mono-diconjugated bilirubin.The unconjugated and albumin-bound bilirubin are the predominant circulatory form of bilirubin in physiological conditions.

The ascertained conditions which alters the bilirubin level in the blood are

A) Protein binding

B) Acidosis

C) Hypoxia

D) Extent of hemolysis.

However, it is uncertain whether these conditions actually modify the cardioprotective potential of bilirubin. Such of the two conditions are briefly explained in the succeeding paragraphs.

1) Factors which modulate Protein bindingare
    a) Albumin concentration in plasma
    b) Drug concentrations which compete on binding
    c) Acidosis.

These factors are expected to affect the balance between bound unconjugated bilirubin instrumental and free (diffusible) form, instrumental in changing the penetration of unconjugated bilirubin into cells.

2) Likewise,membrane integrity is altered by hypoxia. This alteration inmembrane integrity actually modulates transfering capacity of bilirubin.

These complex interactions necessitateto establish the antioxidative capacity of different bilirubin forms. Therefore it is imperative to assess how thebilirubin antioxidative capacity is altered by circulating concentration of blood pH, free bilirubin,circulating albumin and the presence of drugs .

Mechanism responsible for antioxidant activity of Bilirubin:

The chain-carrying peroxyl radical is scavenged by billurubin. This process of scavenging is done by donating a hydrogen atom attached to the C-10 bridge of the tetrapyrrole molecule yielding a carbon-centered radicalBil•

$$LOO\bullet + Bil \rightarrow LOOH + Bil$$

$$Bil\bullet + LOO\bullet \rightarrow Bil\text{-}OOL$$

$$Bil\bullet + O2 \leftarrow\rightarrow Bil\text{-}OO\bullet$$

$$LOO\bullet + BV \rightarrow LOO\text{-}BV\bullet$$

Conjugated bilirubin and unconjugated bilirubin act as antioxidants. This antioxidant property protects human LDL from lipid peroxidation. It is further interesting to note that scavenging activity of bilirubin against peroxyl radicals (generated by 2,2'-*azobis* [2-amidinopropane] dihydrochloride) is established in vitro studies also. H_2O_2concentration to the magnitude of 10,000 and above

isprotected by bilirubin. This action can be done at the concentration as low as 10 nM. Earlier it was believed that α-tocopherol was most effective in preventing lipid peroxidation[20].However,it was established later that bilirubin provides better protection than α-tocopherol in preventing lipid peroxidation under physiologic conditions. Naturally a pertinent question arises as the bilirubin is the abundant endogenous antioxidant. It was established by recent researchers bilirubin is the predominant endogenous antioxidant in mammalian tissues.

The prominent endogenouscytoprotective antioxidantsare glutathione and bilirubin. Bilirubin is an excellent antioxidant in tissues,eventhough the level of bilirubin is thousands times lower than glutathione.This is because of the action of biliverdinreductase which converts biliverdin into bilirubin as soon as biliverdin forms.It has shown that glutathione possess water soluble property protects water soluble proteins from oxidation.On the contrary because of its lipophilic nature bilirubin protects lipids against oxidation. Multiple studies proved that depletion of glutathione &biliverdinreductase augments cell death. A study conducted in mice after deleting heme oxygenase-2, which actually generatesbiliverdin,.Ultimatetly they found glutathione depleted mice showed predominant oxidation of protein, whereas biliverdinreductase deficient showed higher amount of lipid oxidation.

The role of Bilirubin in neonates:

Neonates are not exception to this theory. In newborn infants a linear relationship has been identified between unconjugated bilirubin concentration and its plasma antioxidant capacity. This finding confirmsthat bilirubin is a significant plasma antioxidant.There is also a moderate increase in plasma bilirubin which may be favourableto infants under oxidative stress.

Briemer LH and others found, the breakdown of heme which is a prooxidantmoleculethat yields biliverdin (immediately converted into bilirubin), iron, and carbon monoxide.

The highly active constitutive isoform isHeme Oxygenase-2 in neurons. This accounts for most of the HemeOxygenase activity in the brain. Bilirubin production can be limited by destroying HO-2 gene. This decreased bilirubin production eventually leads to increased oxidative damage following cerebral ischemia[21].

We have already seen that serum bilirubin possess a U-shaped relationship not only with the incidence of ischemic heart disease but also with the outcome of

ischemic heart disease. Significantly bilirubin perfusion is capable of decreasing infarct size caused by IHD. Naturally the upper range of normal values of serum bilirubin concentration protects against the coronary artery disease. Conversely, concentrations in the lower range increase the atherogenicrisk and eventual risk of ischemic heart disease[22].

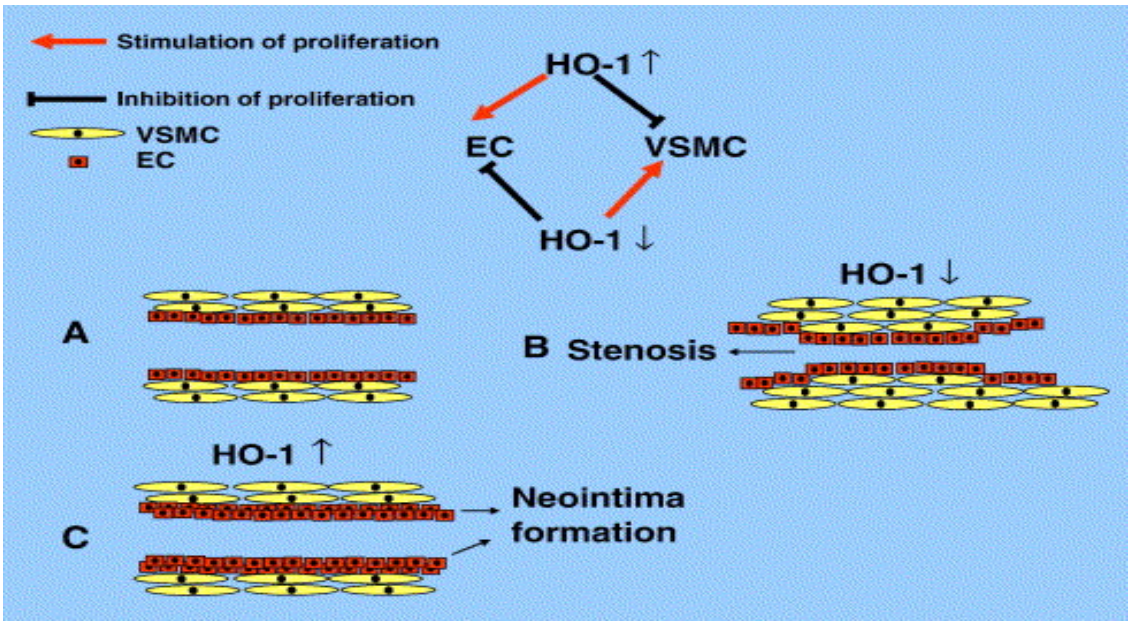
Prevention of Atherosclerosis:

Several mechanisms have been found to be active in the antiatherogenis besides cardio protective effects of bilirubin.The concerned mechanisms are described below:

a)Lipid oxidation inhibition by bilirubin :

Among the Lipoproteins, notably LDL, are extremely prone to oxidation.The uptake of oxidized LDL by intimal macrophages is the key step in atherogenesis.This process eventually results in the accumulation of lipid-rich foam cells. It is possible that bilirubin protects lipids and lipoproteins against oxidation as bilirubin possess anti-oxidant capacity.

The advantage of this process protects the vascularity againstatherogenesis.Therefore low bilirubin concentration is associated with increase in the oxidizedlipoproteins and lipids.This increased oxidation of lipids results in enhancedformation of atherogenic plaque in blood vessels[13,23].



The picture shows the role of HO/CO in stenosis and neointima formation:

(A)decreasein concentration of HO-1 causes vascular smooth muscle cell proliferationthis in turn eventually leads to stenosis.

(B)On the contrary the increased levelof HO-1,prevents neointimal formation by inhibiting vascular smooth muscle cell proliferation.

(C)Healthy tissue is produced by this protective healthy tissue.

b) Enhanced(HO)HemeOxygenase activity of bilirubin:

Increased Hemeoxygenase activity of bilirubin results in antiatherogenic and cardioprotective effects. Hemeoxygenase activity of bilirubinis due to the changes in following metabolites:via

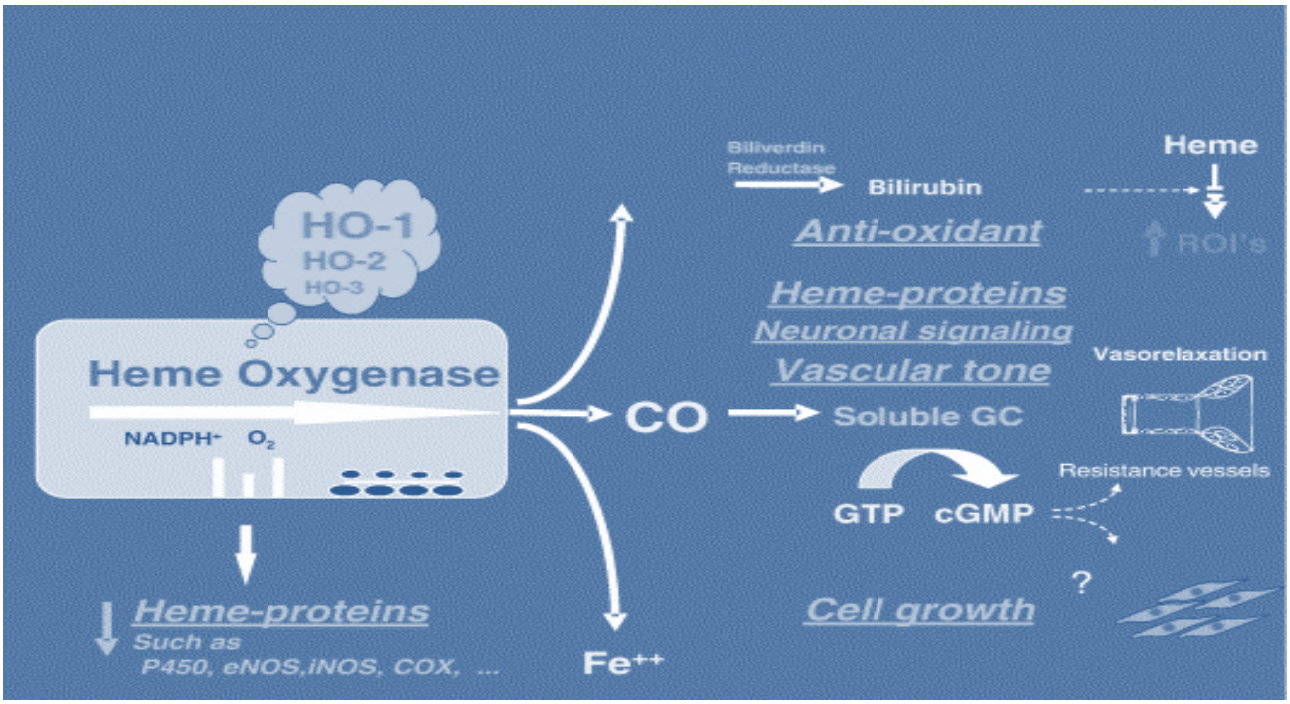
a) increased elimination of heme

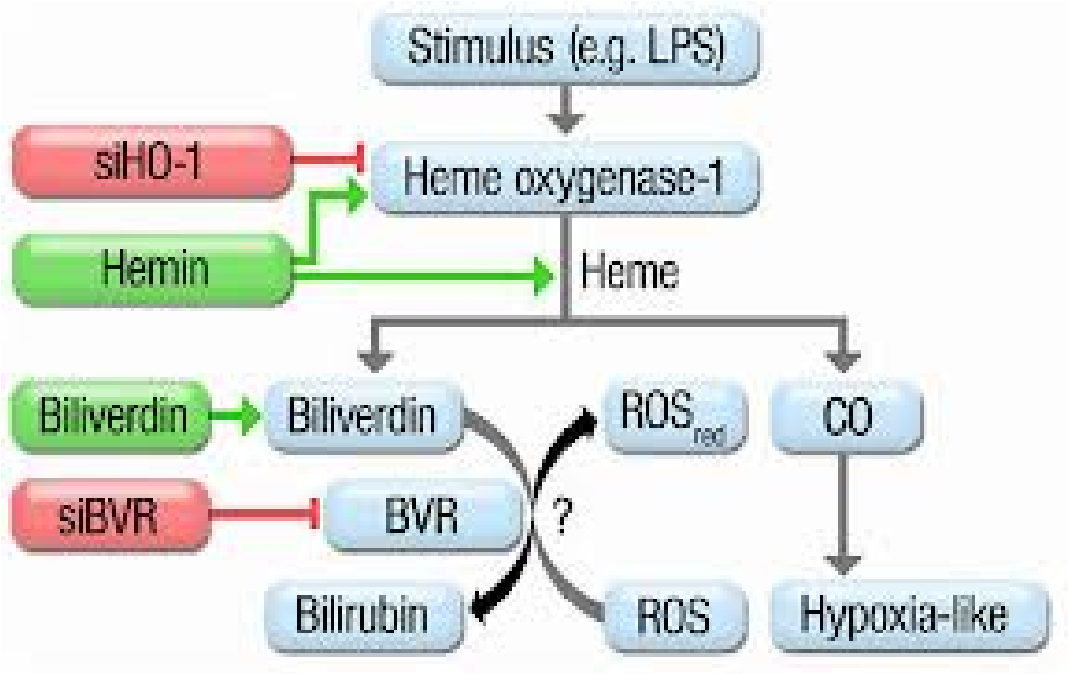
b) enhanced production of CO (Carbon Monoxide)

c) enhanced iron,

d) increased production ofbiliverdin.

Any variation in the concentration of any of the above metabolitesalter the pathophysiology of atherosclerosis[24].For instance, HO-1-mediated consumption of heme reduces toxic cell injury caused by heme. Vasodilatation may be enhanced by decreased hemoglobin concentration.



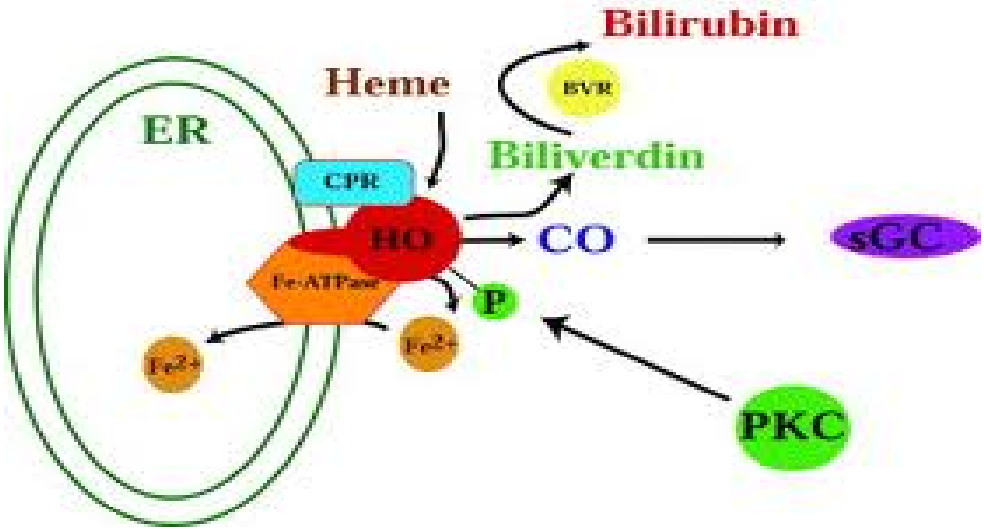


Moreover , hemoglobin being a scavenger of Nitric oxide is capable of blunting nitric oxide dependent vasodilatation.

Role of carbon monoxide:

Carbon monoxide has the characteristic of affecting cardiovascular function through activation of soluble guanylatecyclase.It consequently increases intracellular cGMP concentration. By inhibiting platelet aggregation and vascular smooth

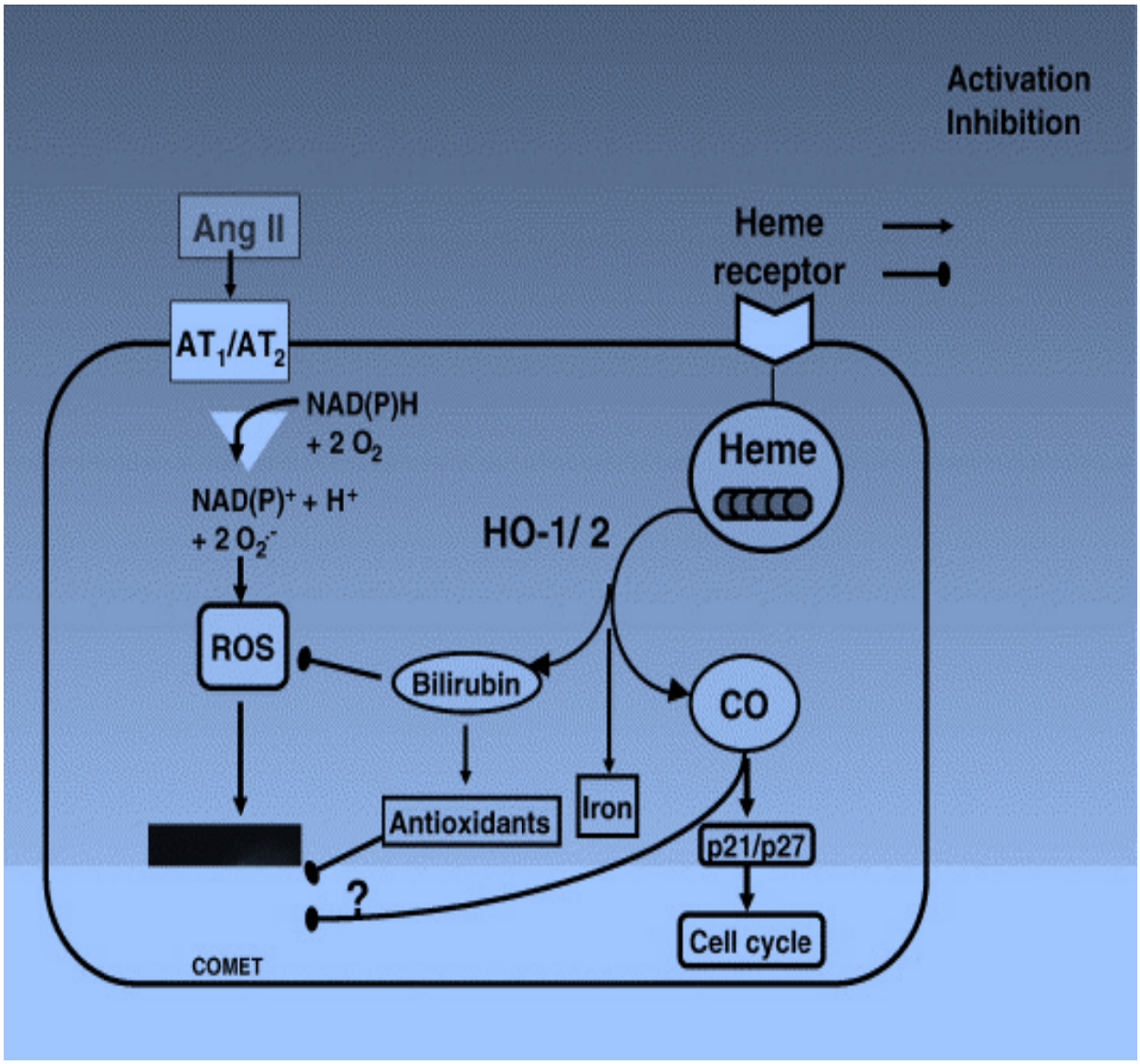
muscle cell proliferation, carbon monoxide acting as a vasodilator which regulates vasomotor tone[25].



Role of hemoxygenase:

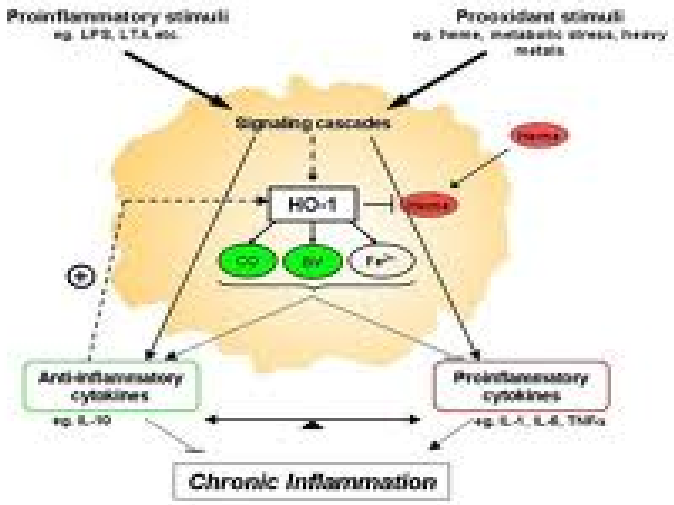
A correlation exists betweenHemeoxygenase -1 activity and coronary artery disease risk.This is substantiated by property of Hemoxygenase -1 which changes the concentration of iron stores by releasing iron[26].This theory has been validated by the study in mice which lacks HO-1 develops anemia.The mice subjected to this study were found to have low serum iron level .And alsoiron was collected in the liver and kidney. These iron stores were found to injure the tissues in the

mice.The oxidative damage inchronic inflammation was found in all HO-1 deficient animals[27].



The above picture shows that increased expression of HO-1not only decreases the cytostatic effects of Angiotensin II but also attenuate degradation of DNA which is measured by COMET assay. p21 and p27 are inhibited by CO which in turn increases cell-cycle progression.Bilirubin inhibitsROS-dependent degradation of DNA.

Balla G and co- workers found that increased expression of ferritinwas due to the induction of Hemeoxygenase by heme[28]. Based on this finding it was further found the synthesis of ferritin was driven by iron released through hemooxygenase activity.The resultant ferritin possesses iron binding capacity.Therefore, endothelial cells are protected from oxidative damages.



a)Immune reactions and inflammatory processes:

Now let us see the association of bilirubin in immune reactions and inflammatory processes, which is a well demonstrated process.In vitro studies by Nakagami found that complement mediated reactions are inhibited by bilirubin and biliverdin[29]. While studying in the guniea pig he further observed that administration of biliverdin inhibits Forssmann anaphylaxis. On the basis of these findings one can easily discerned that bile pigments are endogenous tissue protectors.This was possible because of their anticomplement activity .

Attempts were made to study the existence of relationship between bilirubin metabolism and inflammatory processes.It was found that high HO activity and faster resolution of inflammation are linked together.On the contrary it was observed that the inflammatory responses are potentiated by inhibition of this hemeoxygenase enzyme[30].

Both endothelial and inflammatory cells havenecessary enzymes which are responsible for bilirubin synthesis and degradation[31]. Cellular bilirubin levels are

primarily regulated by these enzymes. This finding establishes a wide physiological role for this endogenous bile pigment in regulating inflammation.

Leukocyte recruitment is mediated by VCAM-1(Vascular cell adhesion molecule-1) which is one of the steps in the process of inflammation. This process of inflammation was observed in number of inflammatory conditions, like atherosclerosis[32,32] and inflammatory bowel disease[34,35].

With regard toatherosclerosis, VCAM-1 is detectable in atherosclerotic plaques.At sites predisposed to atherosclerosis it was found that endothelial expression of VCAM adhesion molecule is an initial event[36].

A study was conducted in the atherosclerotic -prone low density lipoprotein receptor knockout mouse. Where in significant decrease in the number of vascular lesions is noticed due to disruption of VCAM-1 expression.By inhibiting VCAM-1 signaling bilirubin modulates the process of atherogenesis.Several epidemiological analyses conducted by Hopkins, Madhavan establishesan inverse correlation between risk and severity of cardiovascular disease and serum bilirubin level[37, 38, 39,40].

Measuring antioxidant property of bilirubin:

The antioxidant property of bilirubin is measured with the help of ferric reducing ability of plasma. At low PH ferric complex is reduced to ferrous ion which is measured as blue colour with absorption maximum at 593nm.By this assay it was measured bilirubin has antioxidant activity of 4.0, which is double that of uric acid, ascorbic acid,tocopherol. So it was measured that bilirubin protects the gut &liver from oxidative damage. This actually augments the defensing system when other mechanism fails.

Bilirubin and markers of oxidative stress:

Advanced glycation end products(AGEs), such as N-carboxymethyl lysine (CML) or pentosidine, are formed through the interaction ofplasma proteins with sacharide[41] Oxidation productsAGEs activate NF-kB with subsequentoverexpression of proinflammatory genes includingCRP related also to chronic inflammation and correlatewith inflammatory markers, such as CRP, ESR,leukocyte or platelet count[42,43].

Bilirubinvs Inflammation:

Inflammation and oxidative stress are vital in the pathogenesis of atherosclerosis. Multiple studies shown there is a strong inverse correlation between serum bilirubin and highly sensitive C reactive protein (hsCRP).This observation supports the presumption thatatherogenesis is subdued by bilirubin. This action is mediated through inhibition of systemic inflammatory response by bilirubin[44-49].

The anti-inflammatory actions of bilirubin are mediated by the following mechanisms:

- Has anticomplement effects [50]
- Attenuates liver injury in a rat model of endotoxemia[51]
- Blocks oxidant-mediated activation of leukocytes [52]
- Attenuates vascular endothelial proliferation via inhibition of NFkB[53]
- Inhibits transendothelial leukocyte migration via suppression of VCAMsignaling a process implicated in the pathogenesis[54]ofnumerous diseases, includingInflammatory Bowel Disease[55],conjunctivitis[56],nephropathy[57], arthritis[58],systemic collagenoses[59] and possibly cancer[60].

Bilirubin and rheumatological diseases:

There is an inverse relationship between bilirubin levels and various rheumatological disorders.

- Systemic lupus erythematosus,[61]
- Rheumatoid arthritis [62]
- Wegener granulomatosis[63]

There is striking inverse association betweenserum bilirubin levels and SLE.Antioxidant defense systems efficiency is related to theprognosis of patients with SLE[64].Further studies must reveal whether low serum bilirubin levelsare caused by theconsumption of bilirubin during severe SLE-mediated oxidativestress orby the genetic predisposition of affected subjects.65.The same principle might also apply forRheumatoid arthritis andWegenergranulomatosis, where similar results have been detected.

Bilirubin in neurologic andpsychiatric diseases:

Inverse association between serum bilirubin levels andamyotrophic lateral sclerosis [66], depressions[67].The nocturnal bilirubin levels are found to be lower in depression

patient when compared to controls. Serum bilirubin is an important predictor of oxidative stress-mediated diseases including autoimmune, neurologic and psychiatric conditions.

Recent human studies establish that bilirubin has important physiological property because of the fact that higher bilirubin levels correlate with better cardiovascularoutcomes.

In Gilbert's syndrome (UGT1A1):

Mild hyperbilirubinemia occurs in people with Gilbert's syndrome.The prevalence of ischemic heart diseasehas a dubious distinction of having a relatively low percentage (2%)as against thegeneral population (12%)[68].

The gene UGT1A1 codes for a liver specific glucoronosyltransferase that converts bilirubin into a more lipid soluble form the body is able to excrete.Homozygosity at the polymorphic promoter repeat locus UGT1A1 *28 leads to decreased ability of the enzyme to metabolize bilirubin and subsequent mild hyperbilirubinemia[69.]

In patients with Gilbert's syndrome, smaller brachial artery diameter in hyperbilirubinemic patients is consistent with significant decrease in

cardiovascular disease. Brachial artery diameter and to a lesser degree cold pressor test were significantly associated with genotype at the UGT1A1*28 locus, providing compelling evidence that bilirubin affects CVD through pathways associated with artery size such as vasomotor tone,reactivity and possibly arterial wall structure[70].

The Framingham offspringstudy found that higher serum bilirubin levels were associated with lower risk of cardiovascular disease in men.It was also found by same study the subjects who are homozygous for the UGT1A1*28 allele,have higher serum bilirubin levels, eventually decreases the risk of cardiovascular disease[71].

Another study was conducted by LauraJ.Horsfall, Irwin Nazareth, and Irene Petersen in United Kingdom to explore the association between bilirubin and CAD in statin drug using population. In this study they found persons with lower range ofbilirubin(0.06-0.35mg/dl) had higher incidence of CAD compared to higher range of bilirubin(1.1-2.3mg/dl). In comparison patients with 0.3mg/dl bilirubin had 18% higher risk of CAD with a similar CVD risk profile higher bilirubin population(0.6mg/dl).And also they had 34%higher mortality.They conclude that serum bilirubin is an independent risk factor for developing CAD and mortality.

Bilirubin in females:

In females the bilirubin level is not that much reliable because it is affected by estrogen which increases it's metabolism.

Role of bilirubin in peripheral vascular disease:

TheNational Health and Nutrition Examination Survey observed that increased serum total bilirubin level correlates with decrease in the incidence of peripheral arterial disease.Ultimately low serumbilirubin levels correlated with increased carotid intima-mediathickness and impaired flow-mediated dilation which predicts cardiovascular disease in normal healthy individuals. Finally these findings led to the conclusion that increased bilirubin levels decrease the risk of cardiovascular disease in normal subjects[72]. In this study they arrives that 0.1mg/dl increase in bilirubin associated with 6% reduction in peripheral vascular disease.

Smoking vs. serum bilirubin:

Cigarette smoking increases oxidative stress.This oxidative stress increases level of markers of lipid peroxidation in plasma. Smoking induces oxidation of lipids due to exposure to LDL. It also increases the uptake of modified LDL by macrophages. It has already been established that smoking lowers serum bilirubin concentration in males.

Bilirubin is considered tobe a potent antioxidant by inhibiting both lipid and proteinoxidation, under physiological conditions. Oxidative stress and inflammationare fundamental to the arteriopathy. Additionally, bilirubin exerts anti-inflammatory effects on vasculature. Bilirubin is also capable of acting against plaqueformation and eventual atherosclerosis. The association between bilirubin andperipheral artery disease and carotid intima-mediathickness (IMT) is well established doctrine as of today[73-75].

The role ofbilirubin in coronary artery calcification:

People with higher bilirubin concentration are less likely to develop coronary artery calcification (CAC) score. This observation is based on the potential antioxidant and anti-inflammatory properties of bilirubin .Other contributing factors for this action such as oxidative stress, anti-inflammatory role and cellular injuries in atherosclerosis.Recentstudy establishesthat coronary artery calcification score as a newer marker of coronary atherosclerosis. It is a quantitativeobjective measure of coronary artery atherosclerosis.This CAC score is assessed by a noninvasive testmultidetectorcomputed tomography (MDCT). In addition, CAC scoresare related with risk factors for coronaryartery disease and cardiovascular events[76].

Independent inverse associationbetween serum total bilirubin and CAC score in males was inferred from this study.This again emphasis lowserum bilirubin concentration is aoverwhelming risk factor for CAC in males. Moreover, the bilirubin reduces the CAC score by lowering the hsCRP level[77].

Serum bilirubin levels were found to be higher in vegetarians than non – vegetarians. Possibly lower calorie intake may have resulted in higher bilirubin levels because fasting increases bilirubin.

Higher altitudes have been associated with increased bilirubin because of increased hematopoietic response.

In future the extensive research in this field wouldmainly be focuson the following components: viz

- The complex interactions between HO expression,
- The circulating concentrations of its substrate and products,
- The effect of these components, and specifically of bilirubin,
- Bilirubin action on the vasculature,
- Bilirubin role on lipid metabolism
- Bilirubin effect on the cardiovascular system

Which will be cleared in the fore coming years.

AIM

The aim of this study is,to investigate the relationship of serum bilirubin with coronary artery disease patients in comparison with non-coronary controls.

To identify whether any association exists between serum Bilirubin level and the following parameters.

- Age
- Sex
- Blood pressure
- Dyslipidemia
- Diabetes mellitus
- Smoking
- Body mass index
- Family history of CAD

BACKGROUND

SELECTION OF SUBJECTS:

Patients who attended cardiac outpatient department in Kilpauk Medical College Hospital with past history of Myocardial infarction were enrolled in cases after excluding exclusion criteria.

Control subjects are taken from general medicine outpatient department after verifying inclusion and exclusion criteria via questionnaire.

INCLUSION CRITERIA:

Cases: Cardiovascular disease was diagnosed who fulfill the following criteria: Subjects who had

1)Myocardial infarctionevidenced by electrocardiogram (ECG)abnormalities and enzyme changes.

2) Coronary bypass surgery or percutaneous coronary interventions.

3) Significant stenosis on coronary angiogram.

4) An unequivocally positive stress ECG.

Evidence of coronary artery disease within 5 yrs of duration which is confirmed by ECG,ECHO and previous cardiac records are taken as cases.

Controls : Those without CAD matched with age and other co-morbid conditions are taken as control subjects.

EXCLUSION CRITERIA

- Known liver disease
- Acoholism
- Fever with jaundice
- Cerebro vascular accident
- Chronic kidney disease
- Haemoglobin <10g >20g
- Malignancy
- CAD with failure
- Hepatotoxic drug intake
- Hemodynamic instability
- Autoimmune disease
- Chronic obstructive pulmonary disease
- Chronic or current infections
- Use of anti-inflammatory drugs in the past 30days

MATERIALS AND METHODS

Setting:Kilpauk Medical College

Study design: Descriptive analytical study

Period of study: 2010 May -2012 December

Sample size: 200subjects (100 cases + 100 controls)

This study is to compare the serum bilirubin level between CAD and non CAD subjects and its significance among them.And also to identify whether any association exists between age, sex, blood pressure, dyslipidemia,diabetes,smoking and CAD with serum bilirubin level.

Both cases and controls are investigated by following measures.

1) History –duration of CAD, symptoms,family history of CAD,smoking,alcohol intake,past history of jaundice were asked.
2) General examination
3) Systemic examination
4) Blood pressure by sphygmomanometer
5) Body mass index calculation
6) Complete blood count
7) Renal function test

8) Complete Liver function test including serum Total bilirubin,Direct bilirubin,Indirect bilirubin,liver enzymes (AST,ALT,SAP),Total protein ,Albumin,Globulin.
9) Viral markers HBsAg, HCV IgM
10) Fasting lipid profile (Total cholesterol,LDL,HDL)
11) 12lead ECG
12) ECHO –in transthoracic ECHO LV dysfunction,LV hypertrophy,ejection fraction ,valve sclerosis,calcification are noted.

Biochemical analysis

After an overnight fast, blood samples were taken in the morning. Total plasma cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were analyzed in laboratory. With the help of Friedewald formulaLDL-Cholesterol was calculated.

Total serum bilirubin was measured in the laboratory by spectrophotometry method. In the Jendrassik-Grof allied methods, total bilirubin (including direct bilirubin) is reacted with diazotized sulfanilicacidin an acidic medium to form azobilirubin. In theabsence and in the presence of “accelerator” substances mostcommonly caffeine and sodium benzoate, althoughseveral others have been proposed -direct and totalBilirubin, respectively, are quantified.

The absorbance of theazopigment thus developed is then measured as such fordirect bilirubin, or, for total bilirubin, after treatment withalkaline tartrate solution, which shifts the absorption maximumof the azopigment toward longer wavelengths.

DATA ANALYSIS:

Statistical analysis

Mean values of all parameters in subgroups were calculatedby independent sample-t-test. To compare the distributions of dichotomous data viz .,gender, smokers, presence of hypertension or diabetes and bilirubin levels , Chi-square testwas used . Association between CVD and bilirubin levelwas assessed by logistic regression model. Potential confounders, i.e., hypertension, diabetes, age, gender ,body mass index (BMI), HDL-C and TG were adjusted .

Pearson correlations were applied to evaluate the correlation between absolutechanges in bilirubin,AST,ALT,Age,sex,BMI,Hypertension,Diabetes mellitus,lipid profile.

All statistical analyses were performed using the SPSS(software package used for statistical analysis) package .A p-value of less than 0.05 was considered to be statistically significant.

OBSERVATION ANALYSIS

SEX GROUP

Crosstab

			GROUP		Total
			Cases	Control	
SEX	F	Count	28	43	71
		% within SEX	39.4%	60.6%	100.0%
		% within GROUP	28.0%	43.0%	35.5%
		% of Total	14.0%	21.5%	35.5%
	M	Count	72	57	129
		% within SEX	55.8%	44.2%	100.0%
		% within GROUP	72.0%	57.0%	64.5%
		% of Total	36.0%	28.5%	64.5%
Total		Count	100	100	200
		% within SEX	50.0%	50.0%	100.0%
		% within GROUP	100.0%	100.0%	100.0%
		% of Total	50.0%	50.0%	100.0%

Table 1

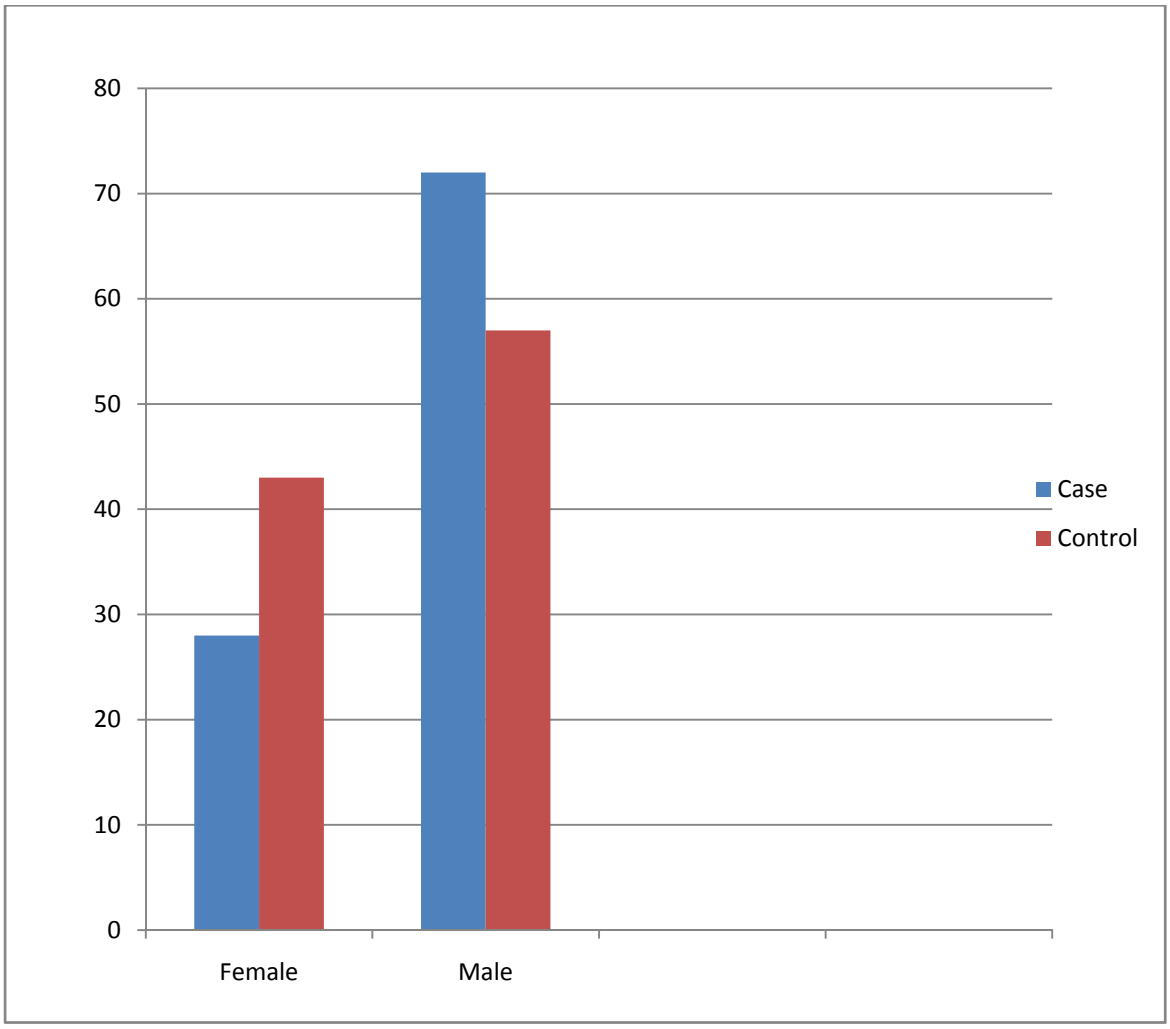


Fig 1

In this study the total no of males contribute 64.5% .females 35.5%.In cases males are higher 36%,females 14%. But in controls females are 21.5%, males 28.5%.There is significant difference in in age group in cases and controls. The P value is 0.027. Males are significantlyhigher in cases, shows higher incidence of cardiovascular disease in males.

DM GROUP

			GROUP		Total
			1	2	
	DM	Count	27	26	53
		% of Total	13.5%	13.0%	26.5%
	Non-DM	Count	73	74	147
		% of Total	36.5%	37.0%	73.5%

Table 2

The diabetic patients in this study group is 26.5%.in cases 13.5%.incontrols 13.0%.the difference in diabetes population between cases andcontrol are not significant.

The above finding is shown in the following graph :

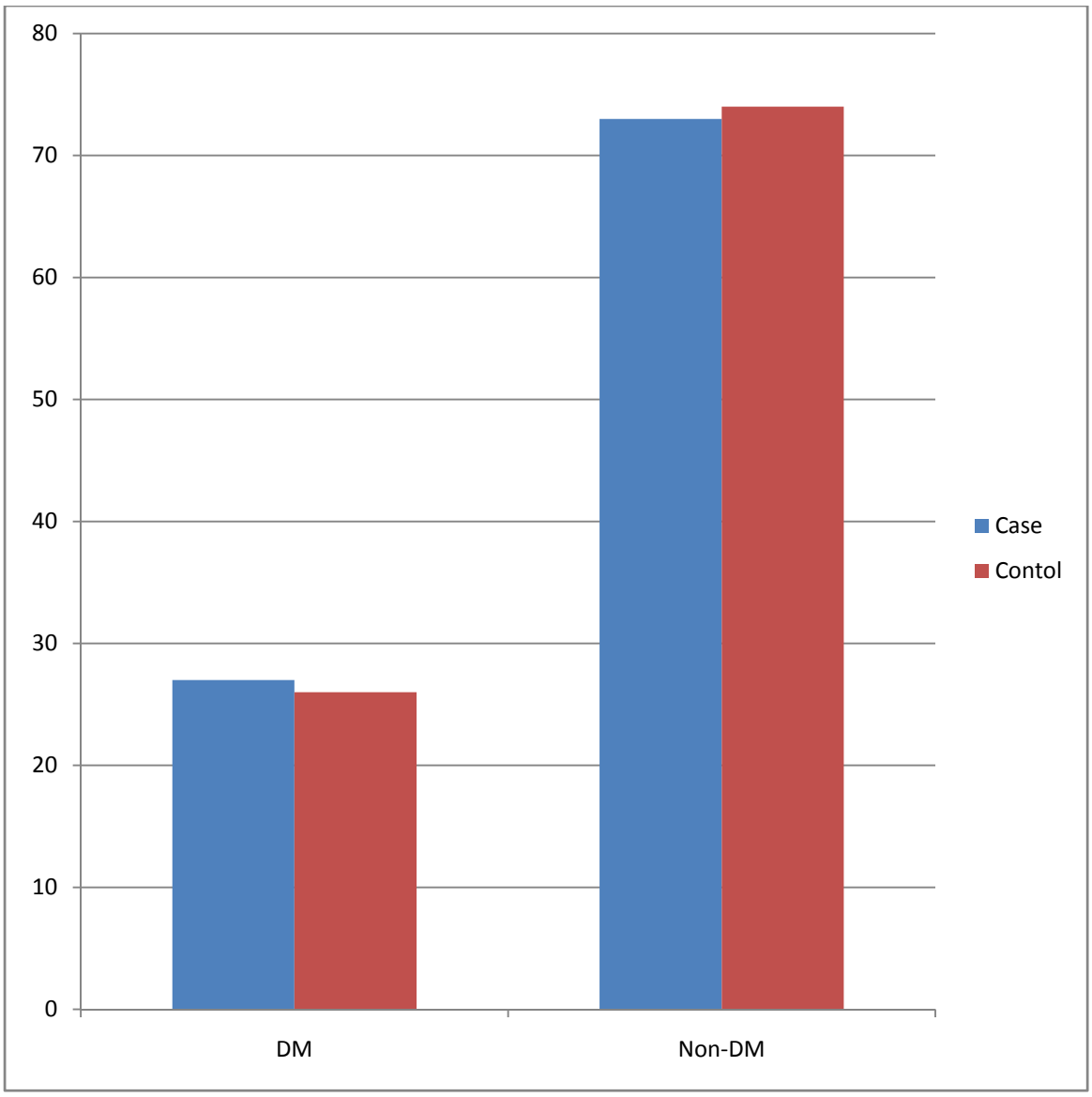


Fig 2

HYPERTENSION GROUP

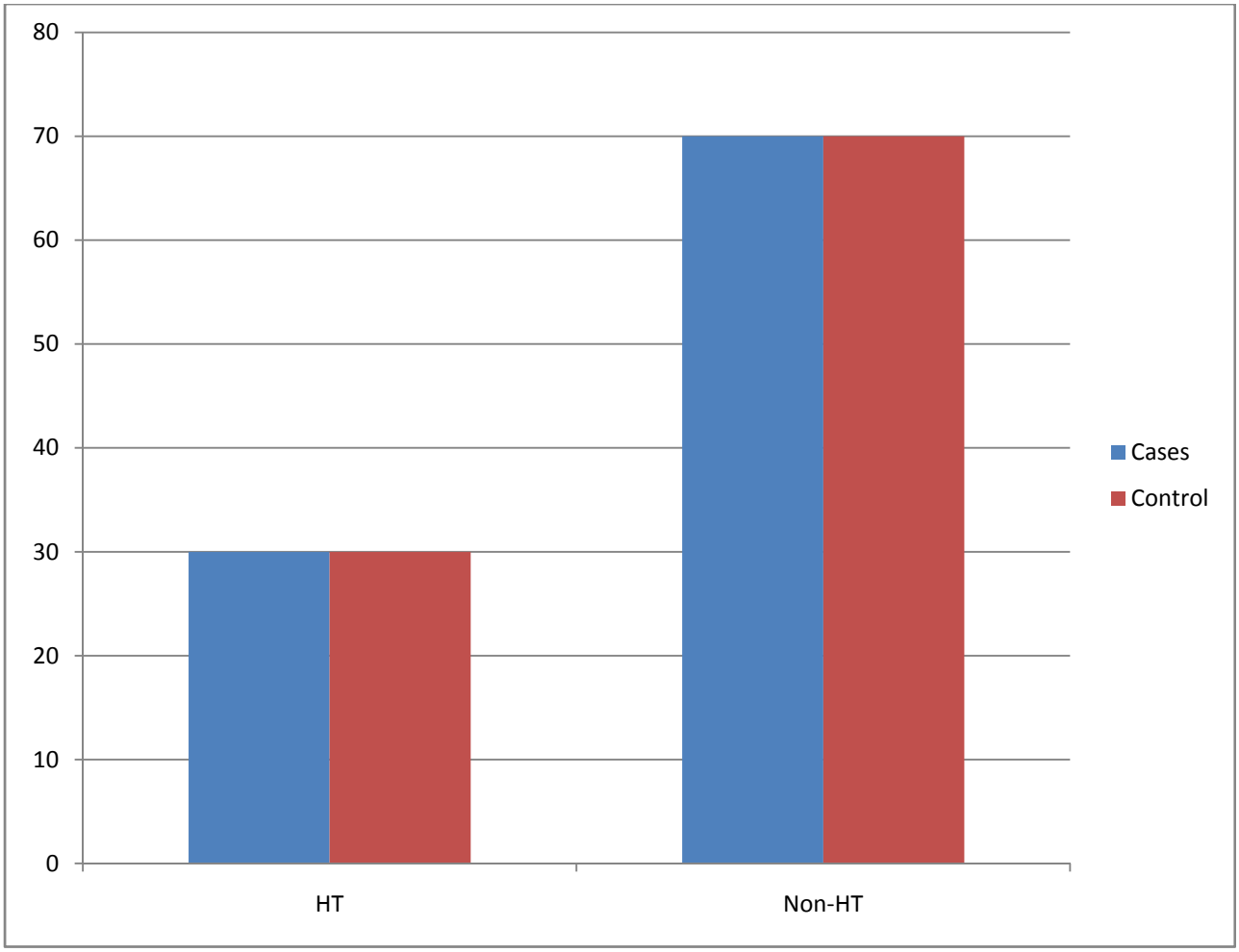


Fig 3

In this study hypertensive population is 30%.each contributes 15%.there is no significant difference between two groups.

FAMILY HISTORY OF CAD

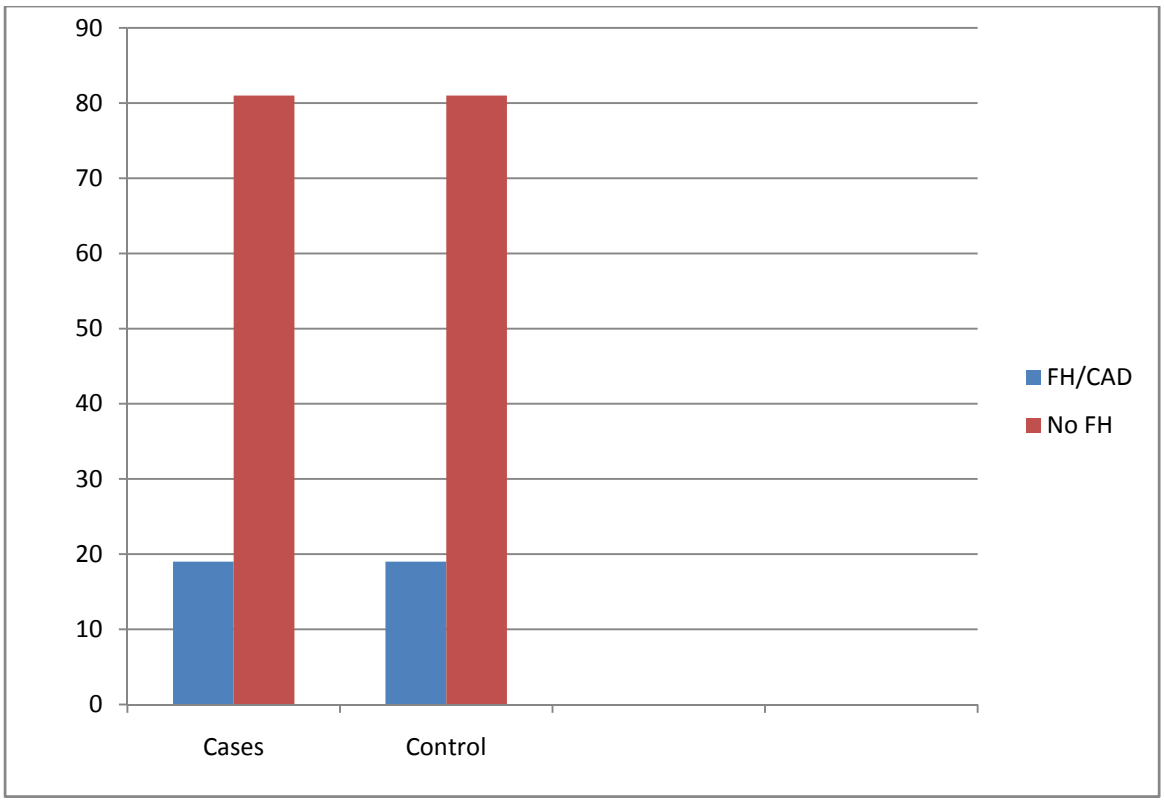


Fig 4

The family history of CAD is present in 9.5% of cases, 9.5% of controls. There is no difference in regards to family history.

SMOKING GROUP

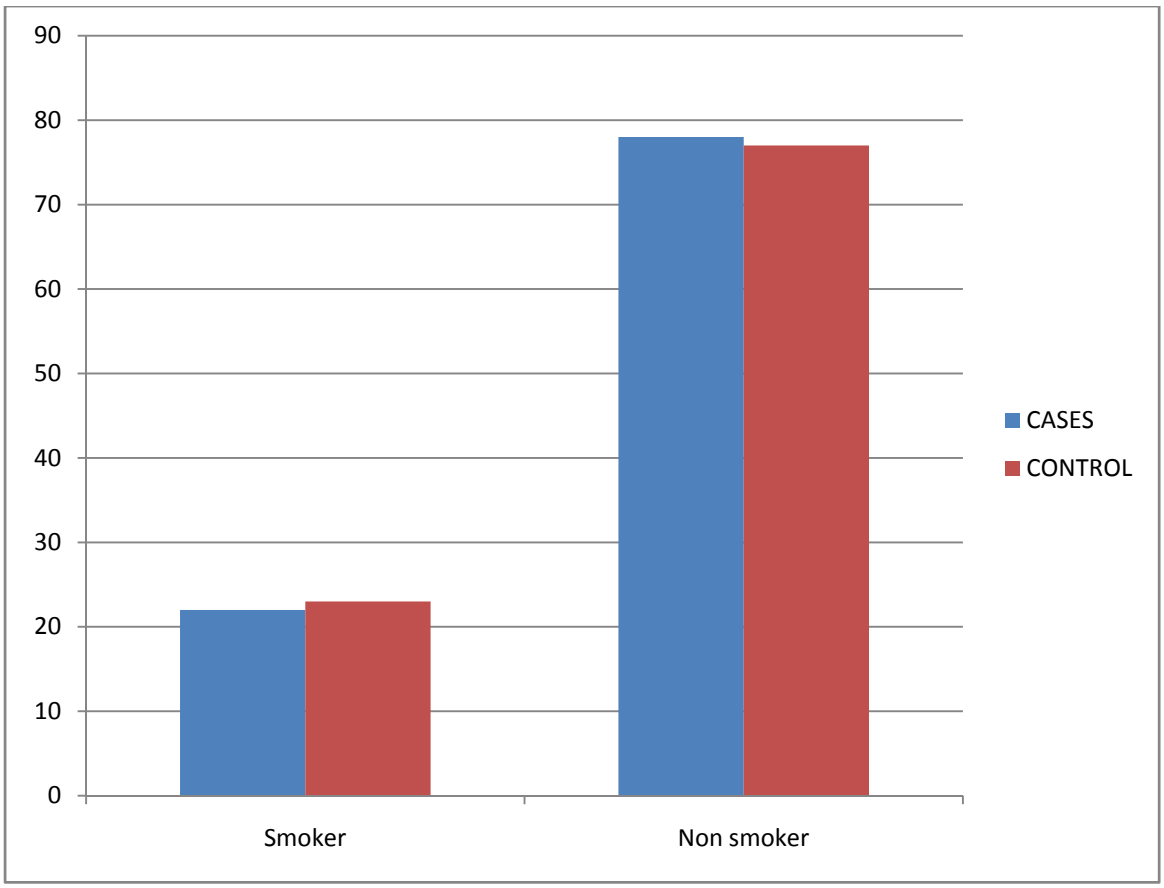


Fig 5

In cases smokers are 11%. In controls smokers 11.5%.overall in this study smokers are 22.5%. non smokers are 77.5%.there is no significant difference between two groups.

TYPE OF MI GROUP

Type of MI	No.of Cases	Percentage
AWMI	72	72%
IWMI	28	28%

Table 3

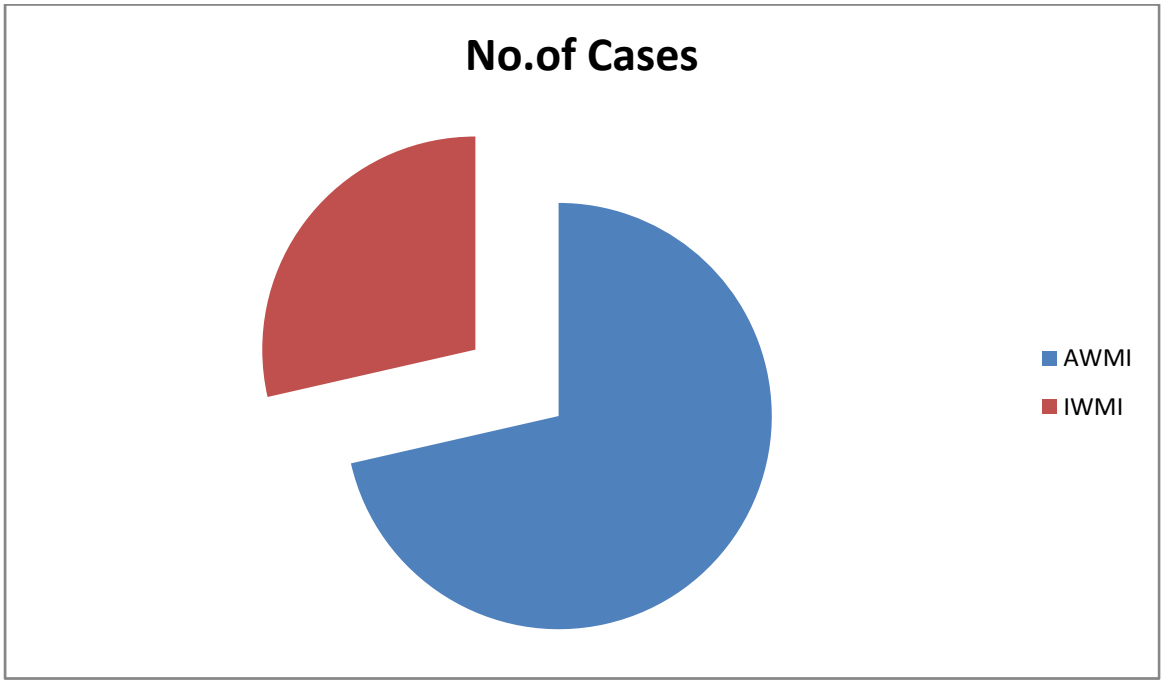


Fig 6

In cases anterior wall MI is more common than inferior wall MI

THE MEAN VALUES

Table 4

AGE MEAN VALUE					
	GROUP	N	Mean	Std. Deviation	Std. Error Mean
AGE	1	100	61.87	15.913	1.591
	2	100	56.47	11.026	1.103

Table 5

		Sig. (2-tailed)	Mean Difference
AGE	Equal variances assumed	.006	5.400
	Equal variances not assumed	.006	5.400

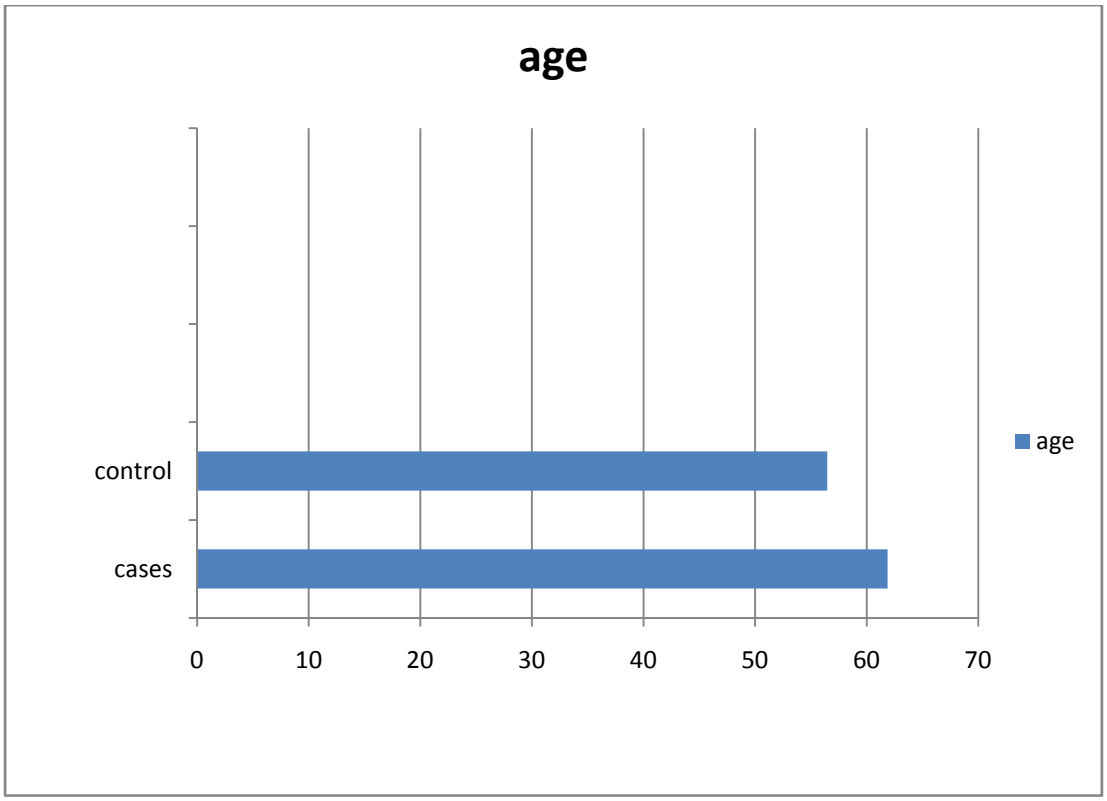


Fig 7

The mean age level of Group 1 and Group 2 are statistically significant.

The p value is 0.006.the mean age in cases is 61.87, in control 56.47.in

cases people are elder than control group.

DURATION OF CAD

Table 6

GROUP	N	Mean	Std. Deviation	Std. Error Mean
DURATION OF CAD	100	3.16	2.642	.264
		.	.	.

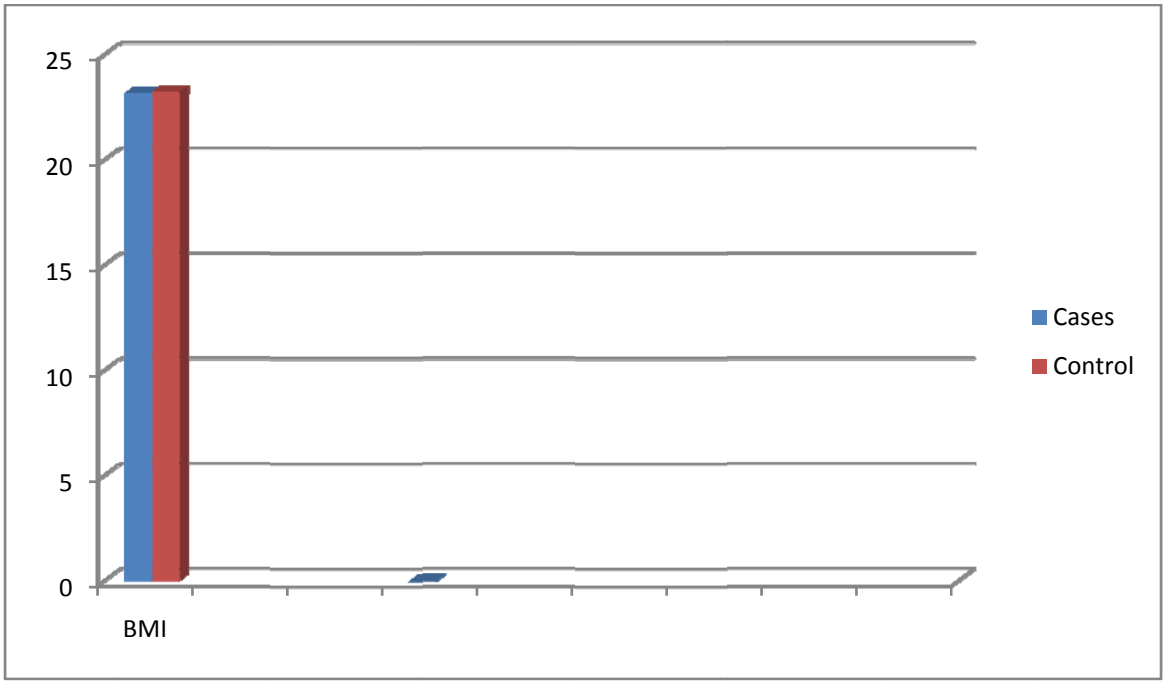
The mean duration of CAD in study group is 3.16 years.

BODY MASS INDEX

Table 7

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
BMI	1	100	23.17	4.379	.438
	2	100	23.23	3.334	.333

Fig 8

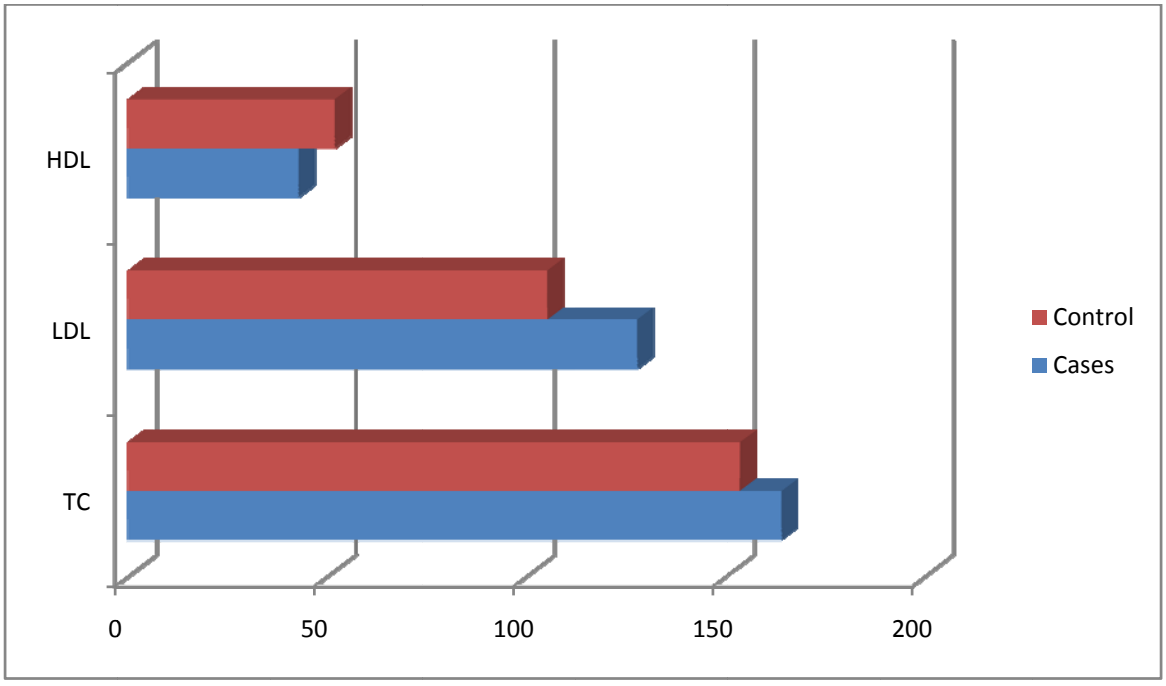


The difference in BMI are not statistically significant. The average BMI in both cases and control is around 23.5

LIPID PROFILE **Table 8**

	GROUP	N	Mean
TC	1	100	163.95
	2	100	153.49
LDL	1	100	127.92
	2	100	105.42
HDL	1	100	42.96
	2	100	52.06

Fig 9



LIPID PROFILE		Sig. (2-tailed)
TC	Equal variances assumed	.002
	Equal variances not assumed	.002
LDL	Equal variances assumed	.000
	Equal variances not assumed	.000
HDL	Equal variances assumed	.000
	Equal variances not assumed	.000

Table 9

The difference of LDL,HDL,Total cholesterol between cases and control are statistically significant. In cases patients are having higher total cholesterol,LDL and low HDL.In controls HDL level are higher,and low LDL,total cholesterol.

LIVER ENZYMES

Table 10

	GROUP	Mean
AST	Cases	10.83
	control	11.00
ALT	cases	11.61
	control	10.94

The difference in AST and ALT are not significant between cases and controls.

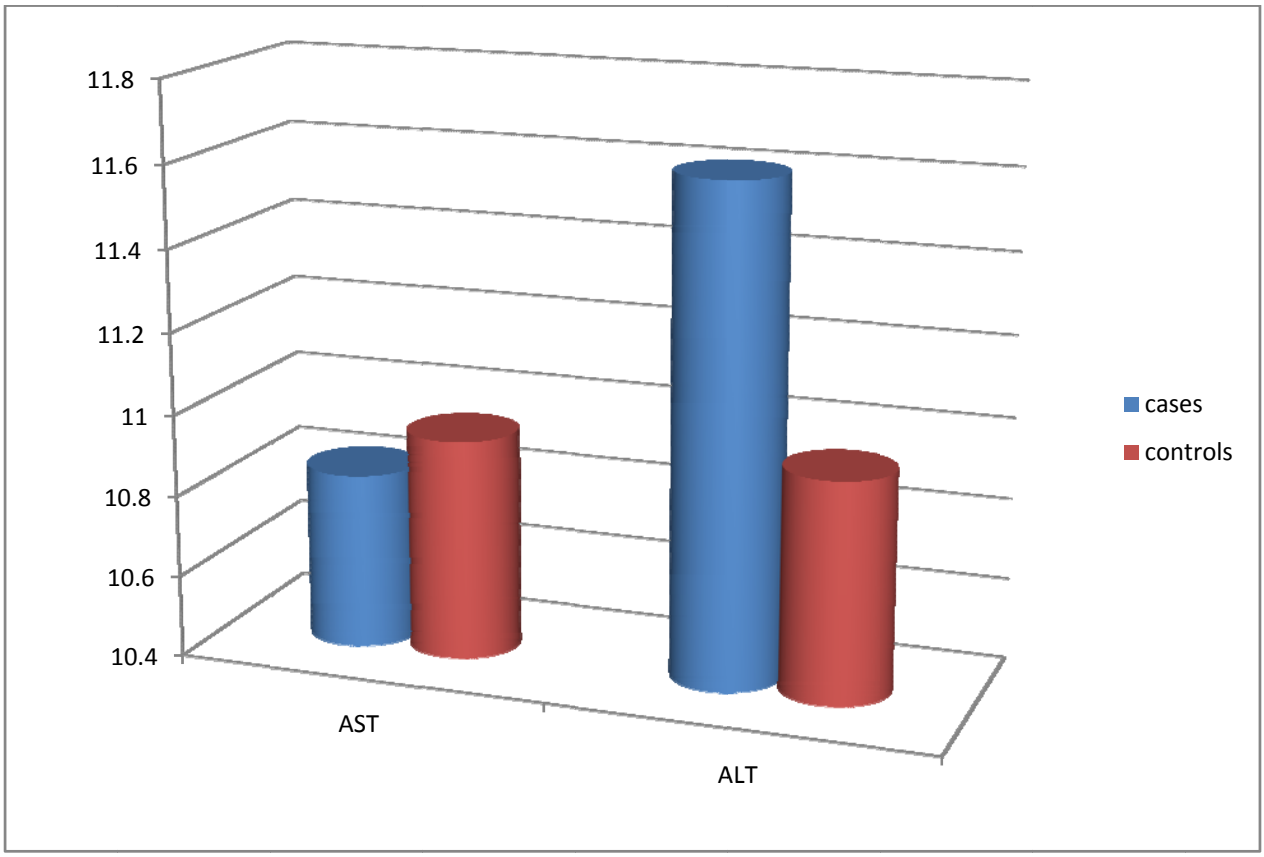


Fig 10

The difference in AST and ALT are not statistically significant between cases and controls.

TOTAL BILIRUBIN **Table 11**

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
TB	1	100	.4774	.15212	.01521
	2	100	.8967	1.74076	.17408

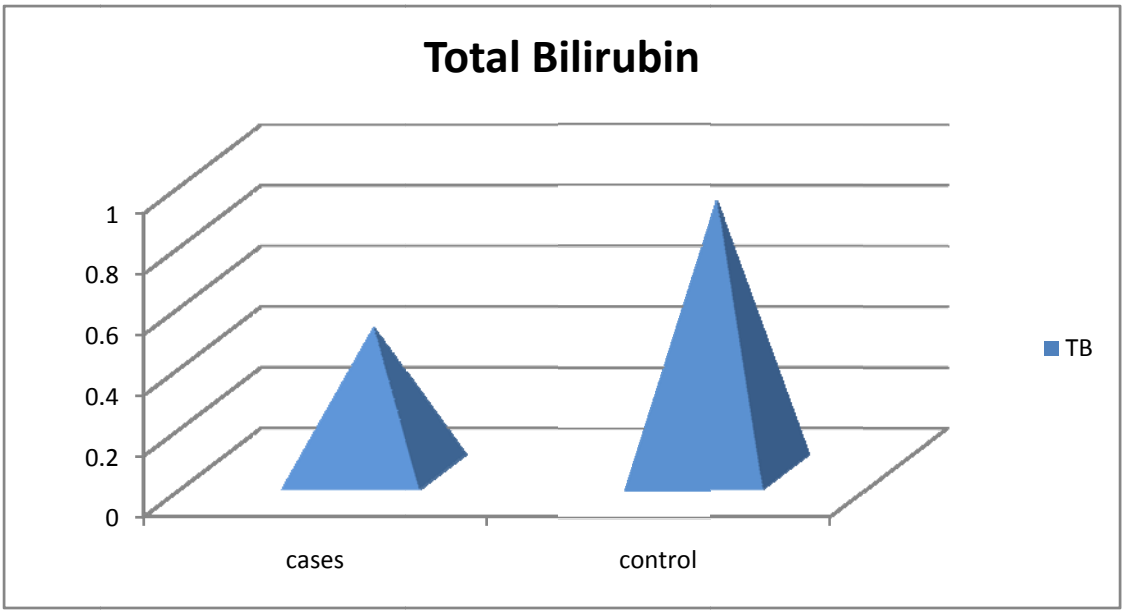


Fig 11

The mean value of serum bilirubin in cases 0.477mg/dl

The mean value in serum bilirubin in controls 0.896mg/dl

Table 12		Sig. (2-tailed)	Mean Difference
TB	Equal variances assumed	.017	-.41930
	Equal variances not assumed	.018	-.41930

The difference in serum total bilirubin between cases and control are statistically significant.The P value is 0.017

DIRECT BILIRUBIN **Table 13**

	GROUP	N	Mean	Std. Deviation
DB	cases	100	.0787	.08183
	control	100	.0786	.08182

The mean value of direct bilirubin between cases and control are not significant.

Table 14

		P value
DB	Equal variances assumed	.993
	Equal variances not assumed	.993

INDIRECT BILIRUBIN

	GROUP	N	Mean
IB	cases	100	.4047
	Control	100	.3900

Table 15

The mean value of indirect bilirubin between cases and control are notstatistically significant.

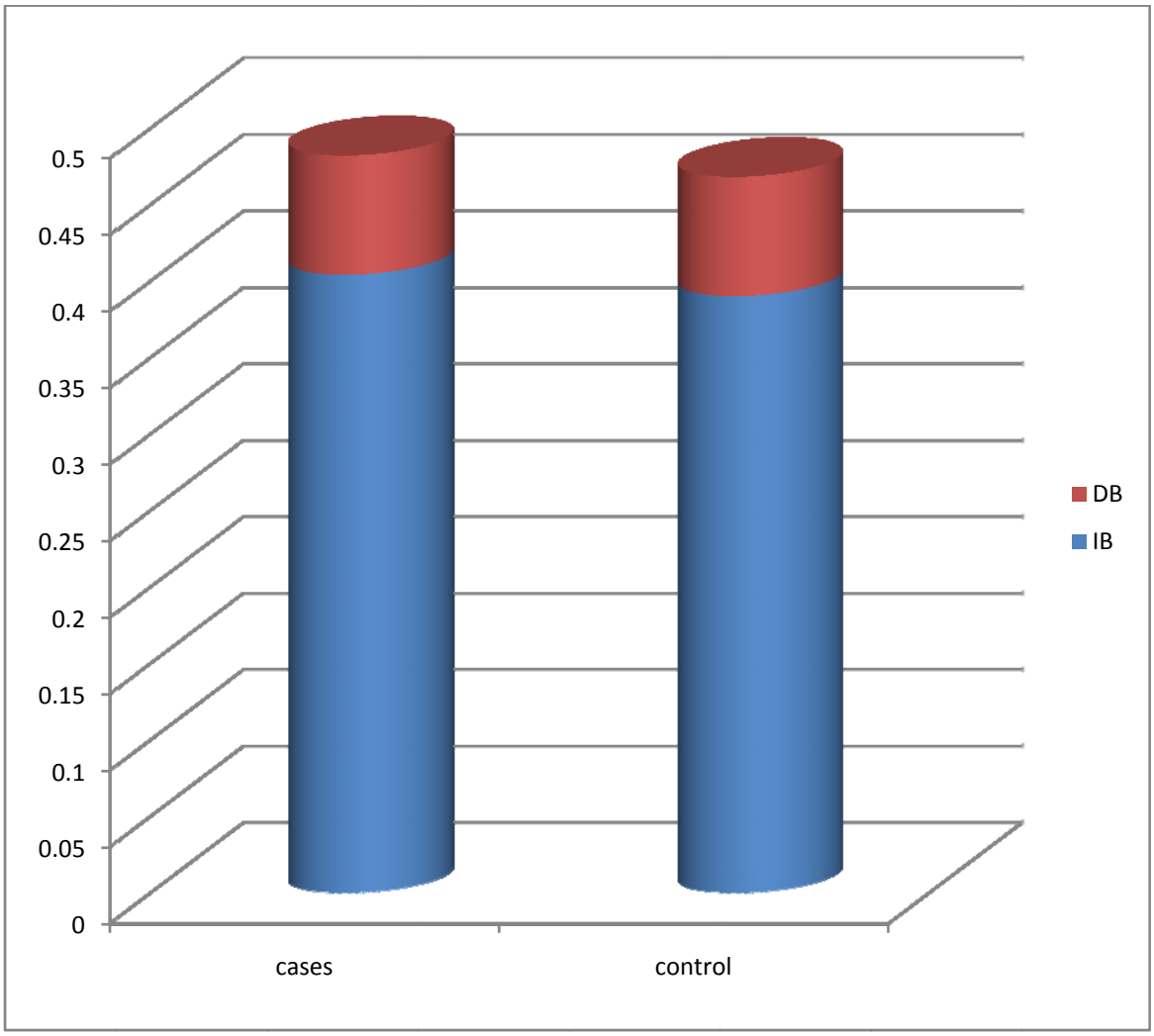


Fig 12

The mean value of direct and indirect bilirubin between cases and control are not statistically significant.

BILIRUBIN IN RELATION WITH SEX:

	SEX	N	Mean
TB	M	72	.4824
	F	28	.4646
DB	M	72	.0833
	F	28	.0668
IB	M	72	.4053
	F	28	.4032

Table16

In association with sex and age there is no significant difference in serum bilirubin.

ASSOCIATION OF SERUM BILIRUBIN WITH DIABETES MELLITUS

	DM	N	Mean
TB	1	27	.4907
	2	73	.4725
DB	1	27	.0785
	2	73	.0788
IB	1	27	.3870
	2	73	.4112

Table 17

There is no significant difference in serum bilirubin between diabetes and non diabetes population.

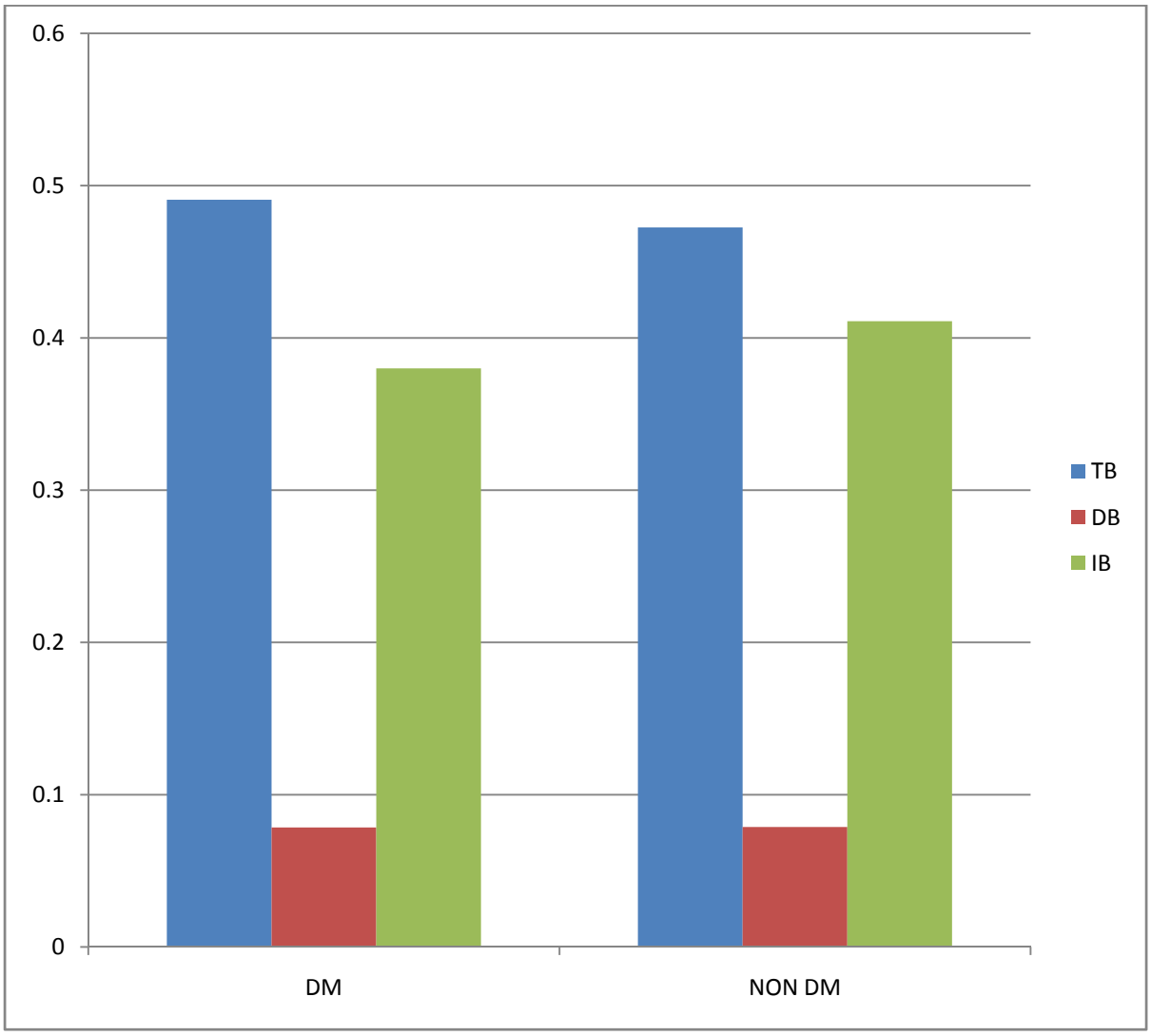


Fig 13

The difference in serum bilirubin between diabetes and non-diabetes populationis not statistically significant.

BILIRUBIN LEVEL IN HYPERTENSIVE POPULATION

	HT	N	Mean
TB	1	30	.4203
	0	70	.5019
DB	1	30	.0537
	0	70	.0894
IB	1	30	.3660
	0	70	.4213

Table 18

		P value
TB	Equal variances assumed	.013
	Equal variances not assumed	.003
DB	Equal variances assumed	.045
	Equal variances not assumed	.004
IB	Equal variances assumed	.057
	Equal variances not assumed	.018

Table 19

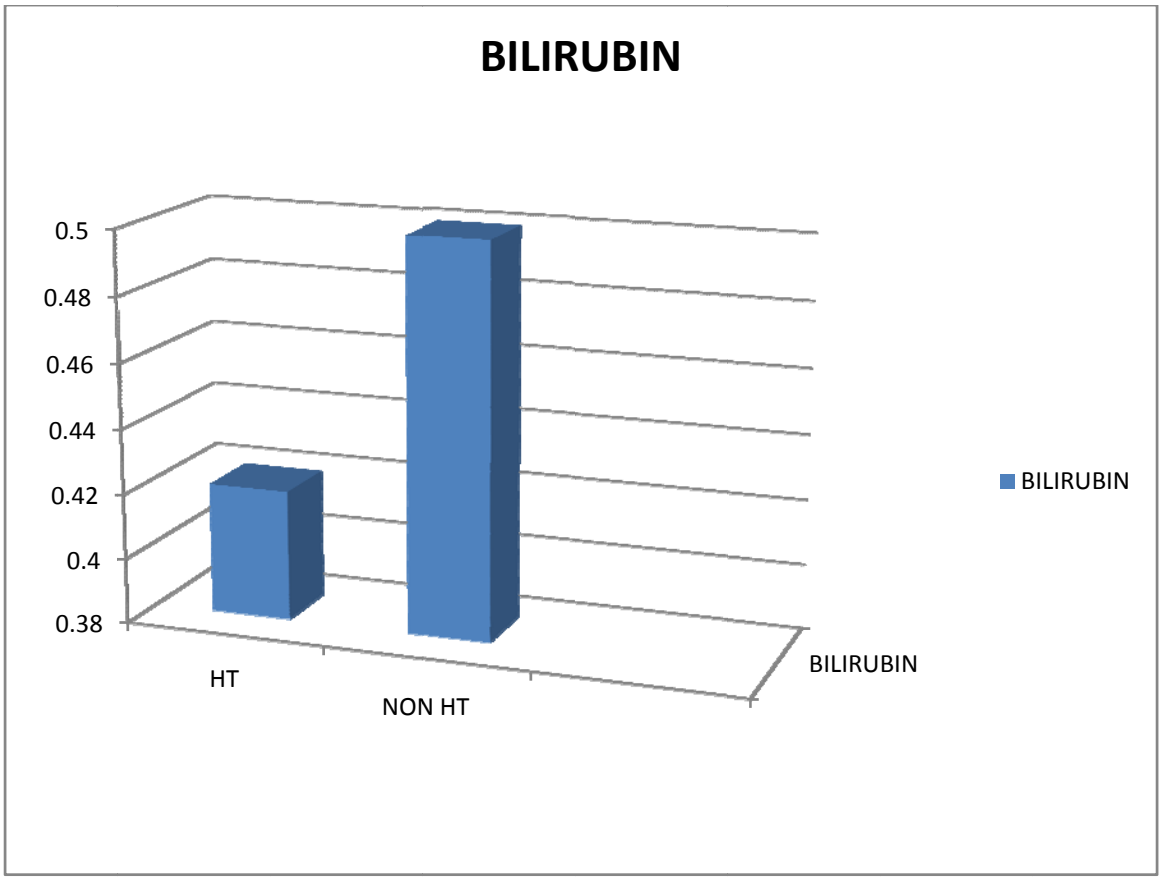


Fig 14

In respective with hypertension the association between hypertension and serum bilirubin is statistically significant.the mean value of serum bilirubin in hypertensive group is 0.42,the mean value in non hypertensive population is 0.50.the difference is significant at level of P value 0.013

FAMILY HISTORY OF CAD WITH SERUM BILIRUBIN

Table 20

	FH/CAD	N	Mean
TB	1	19	.4368
	0	81	.4869
DB	1	19	.0674
	0	81	.0814
IB	1	19	.3800
	0	81	.4105

There is no significant association between family history of CAD and serum bilirubin.

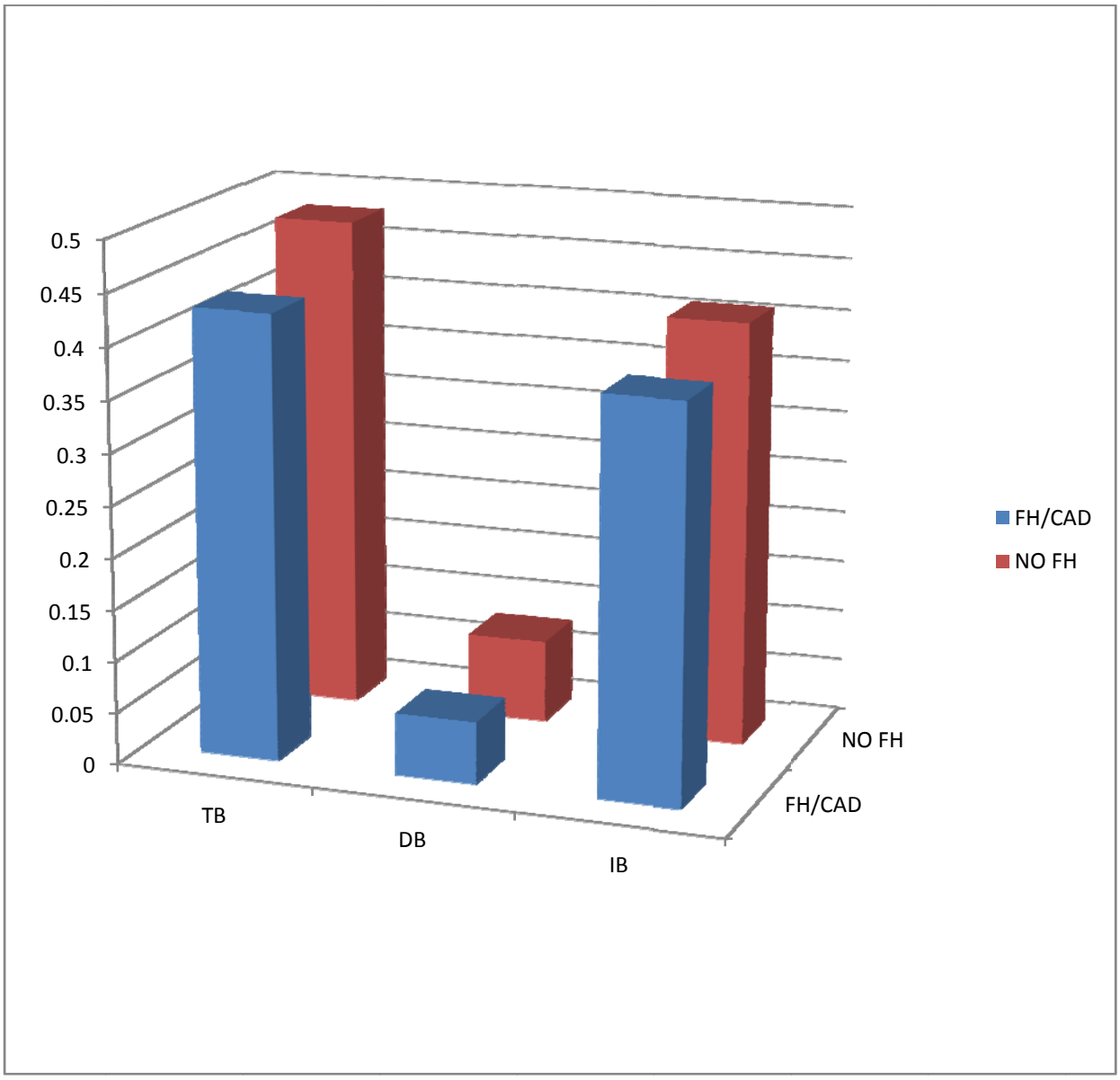


Fig 15

There is no significant association between family history of CAD and serum bilirubin.

SERUM BILIRUBIN LEVEL IN SMOKERS

Table 21

	SMOKING	N	Mean
TB	1	22	.4541
	0	78	.4840
DB	1	22	.0709
	0	78	.0809
IB	1	22	.4086
	0	78	.4036

The mean serum bilirubin in smokers are 0.45, the mean level in non smokers 0.48 .the serum bilirubin levels are lesser in smokers than non smokers. But the difference is not statistically significant.

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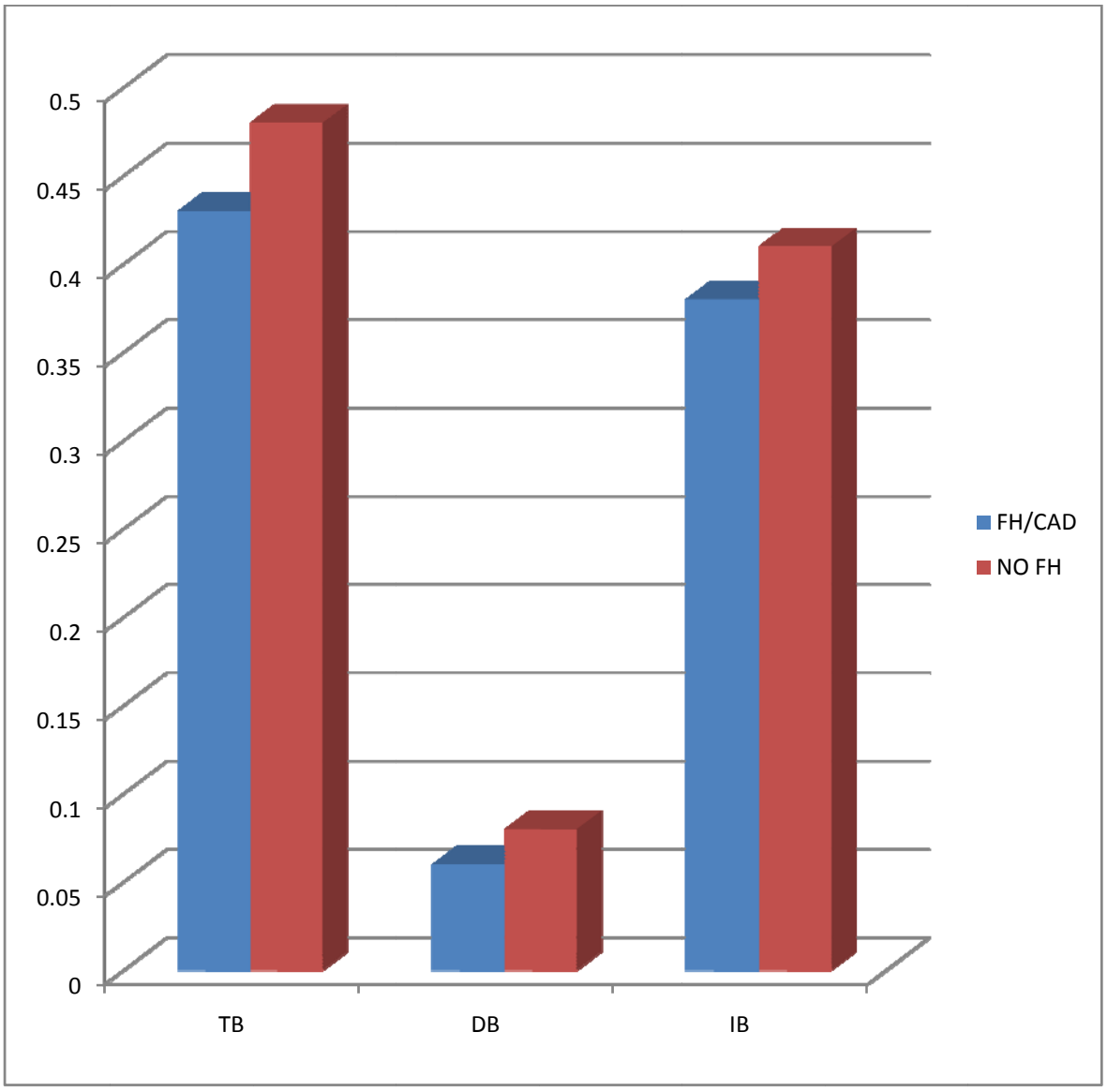

Fig 16

The difference of serum bilirubin in smokers vs non-smokers are not statistically significant.

CORRELATION STUDY:

By analysing with Pearson correlation there is an association between the following parameters.

Mean values in cases and control

Table 22

	Mean in cases	Mean in controls
AGE	61.87	56.47
DURATION OF CAD	3.16	-
BMI	23.17	23.23
TC	163.95	153.49
LDL	*127.92*	*105.42*
HDL	*42.96*	*52.06*
AST	*10.83*	*11.00*
ALT	*11.61*	*10.94*
TB	*0.477*	*0.897*
DB	*.078*	*0.786*
IB	*.40*	*0.39*

In conclusion from correlation study is there is significant correlation at 0.01level(pearson correlation) in the following parameters.

BMI	LDL,Direct bilirubin
Total cholesterol	LDL
Total bilirubin	LDL,Total cholesterol

There is significant correlation at 0.05 level in the following parameters.

Indirect bilirubin	TC,LDL
LDL	Direct bilirubin
ALT	Direct bilirubin
Indirect bilirubin	Total bilirubin

Inference from correlation study:

- The body mass index is directly proportional with LDL and Direct bilirubin. Higher the BMI higher the LDL cholesterol and higher the direct bilirubin.

- Those who having higher total cholesterol also having higher LDL cholesterol.

- The level of total bilirubin and indirect bilirubin is directly proportional with LDL cholesterol and total cholesterol.

- LDL cholesterol is correlating with direct bilirubin.

- ALT level is correlating with direct bilirubin level.

- Indirect bilirubin is directly proportion with direct bilirubin.

DISCUSSION AND INTERPRETATION

In this observational study I studied 200 patients .I analysed 100 patients who had coronary artery disease taken as cases, 100 patients who did not have coronary artery disease were taken as control group.

All the patients underwent complete investigation and were analyzed whether any difference in serum bilirubin between cases and controls. Further assessment was done to find any association of serum bilirubin with multiple variables like age,sex,BMI,smoking,diabetesmellitus,hypertension, family history of CAD,duration of MI,type of MI,Lipid profile,Liver enzymes, LV function .

- The mean age in case group is 61.8 years.The mean age in control group is 56.47.the age is significantly higher in cases than control group.
- The average duration of coronary artery disease is 3.16 years.
- The mean body mass index in study group is 23

- Total cholesterol,LDL cholesterol are significantly higher in coronary artery disease patient.
- HDL cholesterol is higher in control group acting as a protective factor.
- The mean AST,ALT between two groups doesn't have any significant difference.
- Male population is higher in coronary artery disease group whereas females are higher in control group which shows higher risk in males
- Diabetes mellitus population in study population is 23.5%.No significant difference between cases and controls.
- 30% of people are hypertensive in study population.There is no significant difference between two groups.
- Family history of CAD is present in 19% of study population.There is no difference between two groups.
- Smoking history is present in 21.5%.there is no significant difference among cases and controls.
- Anterior wall MI was present in 72%,Inferior wall MI was seen in 28%.
- The mean total bilirubin in coronary artery disease patient is 0.47mg.the mean total bilirubin in non-coronary patient is 0.89mg.Case group has significantly lower bilirubin than control group.

- In association with age,sex,BMI, family history,smoking,type of MI,diabetes mellitus there is no significant difference in serum bilirubin between CAD and non- CAD patients.
- The hypertensive population has significantly lower bilirubin than non-hypertensive population.
- By analysing with pearson correlation,body mass index is directly proportional with LDL and Direct bilirubin. Higher the BMI higher the LDL cholesterol and higher the direct bilirubin.
- Those who having higher total cholesterol also having higher LDL cholesterol.
- The level of total bilirubin and indirect bilirubin is directly proportional with LDL cholesterol and total cholesterol.
- LDL cholesterol is correlating with direct bilirubin.
- ALT level is correlating with direct bilirubin level.
- Indirect bilirubin is directly proportion with direct bilirubin.

Our results are consistent with findings[68,69,70] of both retrospective and prospective study. In these studies similar inverse correlation have been shown not only between serum bilirubin concentrations and coronary artery disease, but also between bilirubin and peripheral vascular disease, carotid intimamedia thickness and stroke-Meta analysis by novotynyetal, of eleven studies has shown an inverse and dose dependent relationship between serum bilirubin and different types and severities of coronary artery disease[71,72].

CONCLUSION

I conclude this study with the observation is that coronary artery disease patients are found to have lower bilirubin level. This finding was established when the bilirubin levels in coronary artery disease patients werecompared with non-coronary artery disease patients after matching the confounding factors.Therefore we may draw a irresistible conclusion that bilirubin plays a protective role against coronary artery disease. In other words, the assessment of serum bilirubin could very well be used to foresee the risk of coronary artery disease in case of high risk population. In order to prevent coronary artery disease ,drugs that increase the bilirubin in moderate level be used in future.

Bilirubin is one of a series of endogenousantioxidants.These compounds operate in complex ways modulated by each other. This is possible due to exogenous antioxidant intake, as well as by the amount of oxidant stress experiences. Oxidant stress is believed to cause damage in atherosclerosis. The damage is caused by initiating lesions besides in aiding their progression to clinical events.Thus bilirubin may be working as a factor in the early phase of development ofatherosclerosis.This is so in the period closer to the onset of clinical events too.Plasma bilirubin concentration and coronary artery disease morbidityhave a

distinct inverse correlation and probably have an important clinical and diagnostic implication.

The clinical relevance relates to potential preventive as well as therapeutic approaches. However, the diagnostic relevance emphasis the plasma bilirubin concentration as a provisional new marker of atherogenic risk which can be measured in the clinical laboratory and applied in medical practice.

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PROFORMA

Name: Age: sex:

Place: Occupation:

History:

Time since diagnosis of CAD:

On treatment with:

Diabetes mellitus:

Hypertension:

Past history of Jaundice:

Family history of CAD:

Smoking:

Alcohol:

Examination:

Height: Weight: BMI:

Pallor: Icterus:

VITALS: BP- PR- RR- JVP-

SYSTEMIC EXAMINATION:

CVS: RS:

ABDOMEN: CNS:

INVESTIGATIONS:

Hb% RBS:

Urea: Creatinine:

Fasting serum Biliribin: T- D- ID-

Liver enzymes:AST ALT SAP

Fasting lipid profile:

ECG:Previous: Present:

Chest X Ray:

ECHO:

S.NO	Name	Age	Sex	Duration of CAD (YRS)	DM	HT	Family History	Smoker	BMI	BP	Type of MI	Lipid Profile			Liver	Enzymes	Serum bilirubin			EF
												T.Chol	LDL	HDL	AST	ALT	T	D	ID	
1	Rajagopal	68	M	2.5	2 Yrs	×	×	×	30.27	120/76	AWMI	186	126	38	18	12	0.8	0.5	0.3	60
2	Dhanavel	49	M	4	×	×	×	ˇ	22.36	118/70	IWMI	136	154	42	10	10	0.51	0.11	0.40	55
3	Velu	51	M	1	×	×	ˇ	×	20.5	120/80	AWMI	196	124	48	19	8	0.40	0.08	0.32	50
4	Srinivasan	59	M	1	×	×	×	×	21.0	126/86	AW	176	126	52	10	18	0.52	0.12	0.4	48
5	Ravi	48	M	5	×	×	×	ˇ	23.2	116/72	AW	126	146	38	12	14	0.36	0.08	0.28	50
6	Munusamy	60	M	4	×	×	×	ˇ	25.3	136/80	IW	196	138	43	9	8	0.42	0.11	0.31	60
7	Dhanapal	65	M	5	ˇ	×	×	×	18.6	116/68	IW	126	135	45	13	14	0.38	0.06	0.32	55
8	Heerolol	60	M	4	ˇ	×	×	×	19.5	120/80	IW	135	145	36	10	12	0.46	0.09	0.37	60
9	Parvathy	55	F	3	×	×	ˇ	×	32.8	130/90	AW	196	187	37	13	17	0.33	0.06	0.27	50
10	Muniammal	55	F	3	×	×	×	×	20.5	110/70	IW	116	128	51	8	9	0.68	0.12	0.56	60
11	Meerbai	60	F	4	×	×	×	×	19.8	130/80	IW	178	137	47	13	12	0.58	0.07	0.51	55
12	Murugesan	62	M	2	×	×	×	×	18.7	110/70	AW	250	186	46	10	9	0.60	0.10	0.50	52
13	Perumal	52	M	4	×	×	×	×	20.0	120/80	AW	153	154	63	21	36	0.49	0.09	0.40	55
14	Alagammal	64	F	3	×	ˇ	ˇ	×	30.5	140/80	AW	225	145	38	17	13	0.36	0.06	0.30	54
15	Thomas	44	M	25	×	ˇ	ˇ	×	19.5	146/90	AW	138	106	32	10	9	0.73	0.13	0.60	64
16	Nithyandan	53	M	2	×	×	×	ˇ	19.5	110/70	AW	126	98	53	8	7	0.43	0.05	0.38	60
17	Ebeneser	48	M	1	ˇ	ˇ	×	ˇ	22.0	130/80	IW	186	127	37	12	14	0.39	0.04	0.35	60
18	Egambaram	58	M	1	×	ˇ	×	×	19.0	150/86	AW	225	176	39	8	7	0.54	0.09	0.43	60
19	Pattammal	70	F	5	ˇ	ˇ	×	×	24.3	160/100	AW	169	142	43	9	9	0.31	0.03	0.28	55
20	Rajeswari	56	F	3	ˇ	ˇ	×	×	20.5	130/90	IW	162	117	39	10	12	0.49	0.06	0.43	60
21	Aunasekaran	70	M	5	×	×	×	×	31.6	126/76	AW	182	136	49	8	7	0.38	0.68	0.30	62
22	Gnanavel	58	M	4	×	×	×	×	18.6	130/80	AW	182	146	46	10	12	0.66	0.06	0.60	45
23	Krishnamoorhy	78	M	3	×	×	×	×	32.0	116/70	AW	210	186	37	8	9	0.42	0.05	0.37	55
24	Arunagiri	38	M	1	×	×	ˇ	×	28.0	140/90	IW	132	115	42	12	12	0.56	0.08	0.48	60
25	Murugesan	48	M	2	×	×	×	×	21.0	150/96	AW	187	153	36	7	6	0.32	0.02	0.30	45
26	Rajendran	53	M	5	×	×	×	×	20.0	120/76	AW	226	176	42	8	9	0.39	0.05	0.34	56
27	Eswaran	84	M	5	×	×	×	×	18.6	128/74	AW	176	132	46	9	12	0.47	0.06	0.41	52
28	Elumalai	76	M	3	×	×	×	×	14.6	130/70	AW	118	92	59	10	7	0.63	0.08	0.55	60
29	Pangajam	84	F	4	×	ˇ	ˇ	×	25.0	120/80	AW	159	136	38	9	9	0.36	0.04	0.32	48
30	Ramaya	69	M	5	×	ˇ	ˇ	×	32.6	110/70	IW	192	146	39	8	6	0.28	0.04	0.24	45
31	Rose	63	M	3	×	×	×	ˇ	19.7	120/80	IW	162	142	51	8	17	0.60	0.08	0.52	60
32	Anbumani	70	M	1	ˇ	ˇ	×	ˇ	22.5	136/86	IW	136	96	48	9	12	0.48	0.06	0.42	55
33	Chinnasamy	45	M	0.5	×	ˇ	×	×	21.0	110/70	AW	176	135	32	13	13	0.31	0.03	0.28	50
34	Kalyanakumari	58	F	4	ˇ	ˇ	×	×	31.5	126/74	AW	116	86	45	6	8	0.52	0.07	0.45	60
35	Jone	63	M	4	ˇ	ˇ	×	×	27.6	140/80	AW	189	147	36	12	13	0.39	0.04	0.35	55
36	Kubendran	57	M	3	×	×	×	×	28.5	138/76	AW	142	110	49	10	10	0.44	0.04	0.40	60
37	Natarajan	48	M	2	×	×	×	×	18.7	110/70	AW	179	139	39	7	8	0.43	0.04	0.39	58
38	Karthikeyan	64	M	2	×	×	ˇ	×	21.1	130/76	AW	156	96	49	6	5	0.30	0.03	0.27	52
39	Chakravarthy	64	M	1	×	×	×	×	22.5	156/86	AW	192	112	42	25	30	0.76	0.16	0.60	60
40	Sulthan Begum	58	F	1	×	×	×	×	23.7	100/60	IW	165	127	37	12	13	0.47	0.07	0.40	55
41	Natesan	70	M	1	×	×	×	×	24.8	110/70	AW	112	86	52	7	8	0.68	0.08	0.60	60
42	Sundaraj	63	M	5	×	×	×	×	12.5	120/86	AW	132	114	36	12	12	0.54	0.07	0.43	55
43	Duraisamy	48	M	5	×	ˇ	ˇ	×	38.5	140/90	AW	176	112	42	6	16	0.45	0.05	0.40	60
44	Leelarathi	55	F	2	×	ˇ	ˇ	×	25.4	130/80	IW	167	121	48	10	10	0.52	0.06	0.46	55
45	Kumaravalli	58	F	4	×	×	×	ˇ	26.5	120/70	IW	156	117	35	9	7	0.4	0.10	0.80	60
46	Sundaramoorthy	59	M	3	ˇ	ˇ	×	ˇ	23.5	116/70	AW	213	176	41	10	10	0.37	0.04	0.33	52
47	Thulukanamma	65	F	5	×	ˇ	×	×	20.0	130/74	AW	195	121	45	8	8	0.28	0.04	0.24	45
48	Kuppan	72	M	2	ˇ	ˇ	×	×	25.6	118/70	AW	136	106	46	12	13	0.41	0.03	0.38	48
49	Ismail	64	M	1	ˇ	ˇ	×	×	22.0	124/60	IW	166	136	38	10	10	0.39	0.1	0.29	40
50	Rani	51	F	1	×	×	×	×	24.0	130/76	AW	146	106	45	8	9	0.51	0.07	0.44	50

51	Manikam	52	M	3	x	x	ˇ	x	30.5	120/80	IW	164	126	40	9	9	0.32	0.04	0.28	48
52	Vajravel	78	M	2	x	x	x	x	21.5	120/70	AW	186	137	38	10	10	0.40	0.03	0.37	50
53	Srinivasan	38	M	1	x	x	x	x	35.5	130/80	AW	146	168	42	8	8	0.36	0.02	0.38	55
54	Alagammal	45	F	2	x	x	x	x	22.0	120/80	IW	156	127	38	15	17	0.39	0.03	0.36	45
55	Saraswathi	54	F	1	x	x	x	x	20.5	120/80	AW	168	138	42	9	9	0.41	0.06	0.35	60
56	Ilavanan	48	M	2	x	ˇ	ˇ	x	25.0	130/80	AW	126	98	46	6	6	0.54	0.06	0.48	55
57	Kannaiyan	66	M	1	x	ˇ	ˇ	x	28.2	130/50	IW	172	121	36	10	10	0.37	0.05	0.32	60
58	Sundar	70	M	3	x	x	x	ˇ	21.0	120/80	AW	156	113	42	8	12	0.30	0.02	0.28	55
59	Muhamad	82	M	5	ˇ	ˇ	x	ˇ	25.0	124/74	AW	136	104	45	10	10	0.51	0.03	0.48	55
60	Hajrabeen	68	F	5	x	ˇ	x	x	24.0	110/70	IW	176	124	38	8	8	0.42	0.04	0.38	60
61	Arumugam	72	M	2	ˇ	ˇ	x	x	18.5	120/70	AW	185	137	42	9	9	0.37	0.04	0.33	45
62	Udayakumar	58	M	5	ˇ	ˇ	x	x	25.0	110/70	AW	147	117	45	10	10	0.38	0.08	0.30	55
63	Chitrambalam	45	F	2	x	x	x	x	20.5	120/40	AW	132	106	39	8	12	0.44	0.06	0.38	60
64	Saroja	54	F	1	x	x	ˇ	x	22.0	130/80	IW	176	126	35	12	14	0.40	0.06	0.34	55
65	Chandra	78	F	2	x	x	x	x	19.0	124/74	AW	167	114	42	10	10	0.38	0.04	0.34	48
66	Rajasekar	48	M	5	x	x	x	x	24.0	130/80	AW	197	127	35	9	7	0.42	0.06	0.36	58
67	Ravisankar	54	M	1	x	x	x	x	22.0	120/80	AW	136	98	44	15	17	0.37	0.03	0.34	55
68	Sarangan	63	M	4	x	x	x	x	23.0	110/70	IW	187	122	36	12	12	0.4	0.06	0.34	60
69	Munirathnam	72	M	5	x	ˇ	ˇ	x	21.5	120/70	AW	156	132	42	8	6	0.44	0.04	0.40	58
70	Guruswamy	48	M	4	x	ˇ	ˇ	x	19.5	120/80	AW	134	127	44	10	10	0.34	0.02	0.32	60
71	Meenamma	58	M	2	x	x	x	ˇ	22.1	130/86	AW	157	126	38	9	9	0.36	0.04	0.32	55
72	sindamani	58	F	3	ˇ	ˇ	x	ˇ	20.0	126/76	AW	176	147	34	12	14	0.48	0.06	0.42	60
73	Vetrivel	72	M	4	x	ˇ	x	x	19.5	112/70	IW	165	125	42	8	6	0.42	0.04	0.38	55
74	Andal	52	F	5	ˇ	ˇ	x	x	21.5	120/70	AW	152	107	36	10	10	0.36	0.06	0.30	55
75	Kanagaraj	48	M	2	ˇ	ˇ	x	x	18.5	110/70	AW	136	98	40	6	8	0.40	0.08	0.32	50
76	Kannan	56	M	2	x	x	x	x	20.0	120/80	IW	167	127	48	14	17	0.56	0.10	0.40	60
77	Lakshmi	86	F	4	x	x	x	ˇ	24.0	130/90	AW	159	116	54	20	18	0.64	0.16	0.54	55
78	Kandasamy	64	M	5	x	x	ˇ	x	19.0	130/86	AW	173	129	46	9	8	0.80	0.20	0.60	60
79	Natarajan	52	M	3	x	x	x	x	22.5	120/76	AW	112	86	50	10	10	0.96	0.16	0.80	60
80	Lingusamy	57	M	2	x	x	x	ˇ	24.0	130/80	AW	136	110	54	9	9	0.9	0.10	0.80	58
81	Neelambari	68	F	1	x	x	x	ˇ	19.0	126/76	IW	176	127	48	12	14	0.36	0.06	0.30	55
82	Saroja	48	M	5	ˇ	x	x	x	22.5	128/78	AW	167	111	52	10	10	0.54	0.06	0.48	55
83	Alagesan	59	M	2	ˇ	x	x	x	24.0	130/90	AW	156	142	48	12	10	0.36	0.06	0.30	60
84	Mohan	65	M	5	x	x	x	ˇ	19.0	120/70	AW	165	136	36	10	12	0.42	0.08	0.34	60
85	Babu	57	M	1	x	x	ˇ	x	22.0	110/70	AW	190	112	52	8	9	0.38	0.08	0.50	55
86	Manoharan	65	M	2	x	x	x	x	28.0	130/80	IW	156	102	42	7	8	0.64	0.06	0.58	60
87	Andalammal	70	F	3	x	x	x	ˇ	24.0	120/70	AW	134	100	38	9	10	0.72	0.08	0.64	55
88	Irudayaraj	60	M	5	x	x	x	ˇ	22.2	110/80	AW	176	146	48	12	14	0.38	0.10	0.28	60
89	Ambika	54	F	4	ˇ	x	x	x	25.5	120/86	AW	182	132	54	16	16	0.46	0.06	0.40	55
90	Egambaram	67	M	3	ˇ	x	x	x	19.5	130/70	AW	171	156	42	17	17	0.71	0.11	0.60	50
91	Periyasamy	78	M	2	x	x	x	ˇ	18.0	140/90	IW	146	110	48	9	9	0.34	0.04	0.30	60
92	Nisha	65	F	1	x	x	ˇ	x	22.5	130/70	IW	158	124	52	12	12	0.42	0.10	0.32	55
93	Radhakrishnan	72	M	4	x	x	x	x	24.5	120/80	AW	164	136	42	37	36	0.76	0.16	0.60	60
94	Aravindan	54	M	5	x	x	x	ˇ	28.5	110/70	AW	176	142	36	22	24	0.32	0.06	0.26	55
95	Thiraiseelan	79	M	3	x	x	x	ˇ	30.5	126/90	AW	145	112	34	18	18	0.30	0.06	0.24	45
96	Nandagopal	67	M	2	ˇ	x	x	x	22.0	130/86	AW	180	170	35	12	6	0.38	0.06	0.26	56
97	Kannagi	56	F	1	ˇ	x	x	x	24.5	120/80	AW	154	111	42	8	8	0.46	0.08	0.09	57
98	Periaswamy	76	M	2	ˇ	x	x	x	22.0	112/70	AW	165	125	44	6	12	0.71	0.06	0.45	59
99	Rukumany	69	F	3	ˇ	x	x	x	24.0	120/70	AW	156	138	45	8	14	0.86	0.07	0.67	62
100	kumaraswamy	72	M	4	ˇ	x	x	x	26.0	120/80	AW	165	127	48	6	16	0.88	0.09	0.78	67

S.NO	Name	Age	Sex	DM	HT	Family History	Smoker	BMI	BP	Lipid Profile			Liver	Enzymes	Serum bilirubin			EF
										T.Chol	LDL	HDL	AST	ALT	T	D	ID	
1	Manikandan	56	M	2 Yrs	×	×	×	24.0	120/86	112	152	55	12	11	0.42	0.5	0.3	60
2	Elumalai	66	M	×	×	×	ˇ	22.0	126/60	170	136	35	10	8	0.76	0.11	0.40	55
3	Vijaya	55	F	×	×	ˇ	×	19.5	130/80	170	112	42	8	8	0.32	0.08	0.32	50
4	Egambaram	67	M	×	×	×	×	23.0	110/90	180	85	34	6	10	0.30	0.12	0.4	48
5	Ananavel	56	M	×	×	×	ˇ	20.5	120/80	112	75	36	9	13	0.76	0.08	0.28	50
6	Meena	45	F	×	×	×	ˇ	18.5	130/80	146	86	58	10	9	0.66	0.11	0.31	60
7	Govindammal	60	F	ˇ	×	×	×	22.5	120/80	118	126	48	8	6	0.46	0.06	0.32	55
8	Vijayalakshmi	50	F	ˇ	×	×	×	20.5	120/70	136	112	56	12	10	0.98	0.09	0.37	60
9	Ragavan	75	M	×	×	ˇ	×	22.5	130/80	146	96	52	10	8	0.96	0.06	0.27	50
10	Muthusamy	67	M	×	×	×	×	24.0	120/76	156	117	49	8	12	0.76	0.12	0.56	60
11	Kamala	75	F	×	×	×	×	21.0	130/80	112	96	56	7	8	1.00	0.07	0.51	55
12	Unnamalai	55	F	×	×	×	×	20.5	120/80	124	120	58	12	6	1.00	0.10	0.50	52
13	Munusamy	47	M	×	×	×	×	21.5	130/80	136	107	55	9	10	0.46	0.09	0.40	55
14	Muthusamy	58	M	×	ˇ	ˇ	×	19.5	120/70	176	147	36	12	6	1.20	0.06	0.30	54
15	Dhanabagiyam	62	F	×	ˇ	ˇ	×	21.5	130/86	110	86	68	10	9	0.56	0.13	0.60	64
16	Vasanthakumari	50	F	×	×	×	ˇ	23.4	120/80	196	142	58	8	12	0.90	0.05	0.38	60
17	Anbarasu	47	M	ˇ	ˇ	×	ˇ	21.5	120/70	164	98	45	10	10	0.94	0.04	0.35	60
18	Ezhilarasan	55	M	×	ˇ	×	×	19.5	120/80	146	86	64	8	13	0.74	0.09	0.43	60
19	Lalitha	62	F	ˇ	ˇ	×	×	21.0	110/76	136	118	48	10	10	0.68	0.03	0.28	55
20	Ezhilsundar	38	M	ˇ	ˇ	×	×	24.5	130/80	146	126	58	8	10	0.48	0.06	0.43	60
21	Elamaran	72	M	×	×	×	×	20.0	116/70	179	132	64	6	10	0.68	0.68	0.30	62
22	Rani	57	F	×	×	×	×	24.0	120/74	148	95	58	9	8	0.70	0.06	0.60	45
23	Sachi	67	M	×	×	×	×	22.0	120/70	164	102	46	12	6	0.86	0.05	0.37	55
24	Krishnamoothy	58	M	×	×	ˇ	×	21.5	136/86	136	84	64	10	9	0.36	0.08	0.48	60
25	Annapoorana	40	F	×	×	×	×	21.5	120/76	176	132	32	8	12	0.90	0.02	0.30	45
26	Kuppan	76	M	×	×	×	×	19.5	126/70	154	112	45	10	10	0.68	0.05	0.34	56
27	Balakrishnan	48	M	×	×	×	×	20.5	136/70	140	119	41	8	8	0.86	0.06	0.41	52
28	Malar	40	F	×	×	×	×	21.0	124/74	156	124	54	6	8	0.97	0.08	0.55	60
29	Chinasamy	52	M	×	ˇ	ˇ	×	24.0	120/70	136	94	62	12	14	0.76	0.04	0.32	48
30	Dhamasekar	62	M	×	ˇ	ˇ	×	21.0	120/80	176	142	38	9	8	0.82	0.04	0.24	45
31	Dhanabakiyam	42	F	×	×	×	ˇ	24.5	110/76	156	116	54	14	14	0.90	0.08	0.52	60
32	Chitrambalam	55	M	ˇ	ˇ	×	ˇ	23.0	124/74	142	92	58	10	10	0.45	0.06	0.42	55
33	Thulukannama	72	F	×	ˇ	×	×	20.0	120/70	136	100	45	11	12	1.00	0.03	0.28	50
34	Dhanajeyan	55	M	ˇ	ˇ	×	×	26.5	110/70	148	110	54	8	9	0.7	0.07	0.45	60
35	Mahalakshmi	50	F	ˇ	ˇ	×	×	22.5	120/76	148	106	45	10	11	0.64	0.04	0.35	55
36	Dhamotharan	56	M	×	×	×	×	28.5	130/70	154	98	48	8	8	0.86	0.04	0.40	60
37	Rooparathi	70	F	×	×	×	×	20.0	126/70	174	102	54	10	10	0.96	0.04	0.39	58
38	Marlene Jones	58	F	×	×	ˇ	×	26.5	112/08	164	106	48	12	14	0.48	0.03	0.27	52
39	Esakian	62	M	×	×	×	×	22.0	130/80	194	124	36	8	8	1.02	0.16	0.60	60
40	Fathimabegam	65	M	×	×	×	×	24.5	126/76	164	85	64	12	13	0.68	0.07	0.40	55
41	Gunasekar	40	M	×	×	×	×	35.0	130/70	146	76	58	8	10	0.90	0.08	0.60	60
42	Rajamanikam	54	M	×	×	×	×	21.0	120/74	156	90	52	12	12	0.86	0.07	0.43	55
43	Harikrishnan	65	M	×	ˇ	ˇ	×	24.0	132/72	176	124	48	8	6	1.20	0.05	0.40	60
44	Rangamma	50	F	×	ˇ	ˇ	×	24.5	120/74	142	96	58	12	10	0.60	0.06	0.46	55
45	Chinnadurai	72	M	×	×	×	ˇ	21.0	110/70	136	72	82	6	8	0.94	0.10	0.80	60
46	Lalli	40	F	ˇ	ˇ	×	ˇ	22.0	120/76	148	88	44	7	7	0.88	0.04	0.33	52
47	santha srinivas	55	M	×	ˇ	×	×	24.0	130/70	164	88	49	12	12	0.76	0.04	0.24	45
48	Meenambigai	62	F	ˇ	ˇ	×	×	25.0	120/70	136	72	64	8	8	0.42	0.03	0.38	48
49	Chinnasamy	74	M	ˇ	ˇ	×	×	22.5	110/70	170	106	46	7	7	0.46	0.1	0.29	40
50	Alamelu	60	F	×	×	×	×	19.0	120/80	156	120	48	12	12	0.56	0.07	0.44	50

51	Egavalli	40	F	×	×	ˇ	×	21.0	130/70	146	86	54	8	8	0.76	0.04	0.28	48
52	Palani	54	M	×	×	×	×	21.5	120/80	134	76	86	12	12	0.60	0.03	0.37	50
53	Kandasamy	65	M	×	×	×	×	23.5	120/70	176	142	36	20	20	0.78	0.02	0.38	55
54	Indumathi	46	F	×	×	×	×	20.0	110/70	165	106	48	9	9	0.42	0.03	0.36	45
55	Bharathy	45	F	×	×	×	×	21.0	120/70	132	82	46	8	9	0.86	0.06	0.35	60
56	Sivakami	35	F	×	ˇ	ˇ	×	21.5	124/80	184	106	52	10	12	0.94	0.06	0.48	55
57	Kuppan	72	M	×	ˇ	ˇ	×	23.5	110/78	164	112	54	14	17	0.62	0.05	0.32	60
58	Subramaniyan	65	M	×	×	×	ˇ	20.0	120/76	154	89	64	9	8	0.86	0.02	0.28	55
59	Chellamal	67	F	ˇ	ˇ	×	ˇ	21.5	130/70	178	104	52	7	7	0.94	0.03	0.48	55
60	Gandhi	45	M	×	ˇ	×	×	22.5	140/90	184	116	46	8	8	0.62	0.04	0.38	60
61	Umarani	50	F	ˇ	ˇ	×	×	23.5	120/80	187	142	48	10	10	0.86	0.04	0.33	45
62	Kanniyammal	55	F	ˇ	ˇ	×	×	24.0	112/70	134	86	64	12	12	0.96	0.08	0.30	55
63	Muniyan	45	M	×	×	×	×	21.0	120/80	146	74	54	10	10	1.08	0.06	0.38	60
64	Sivakumar	54	M	×	×	ˇ	×	27.8	130/86	167	142	36	8	8	0.82	0.06	0.34	55
65	Thangavel	75	M	×	×	×	×	28.4	128/70	132	82	62	6	6	0.54	0.04	0.34	48
66	Ganesan	35	F	×	×	×	×	20.5	124/68	148	86	56	7	8	0.78	0.06	0.36	58
67	Sivagami	65	F	×	×	×	×	26.0	124/76	146	80	51	6	8	0.89	0.03	0.34	55
68	Ranganayagi	72	M	×	×	×	×	23.0	132/72	176	126	52	10	12	0.68	0.06	0.34	60
69	Neelakandan	58	F	×	ˇ	ˇ	×	25.0	126/78	158	112	48	14	14	0.56	0.04	0.40	58
70	Ramani	54	M	×	ˇ	ˇ	×	38.5	110/80	148	82	54	20	22	0.48	0.02	0.32	60
71	Balaraman	48	M	×	×	×	ˇ	22.5	120/76	134	96	46	20	17	0.36	0.04	0.32	55
72	Ulaganadhan	52	F	ˇ	ˇ	×	ˇ	24.0	130/74	142	76	50	18	13	0.98	0.06	0.42	60
73	Veeralakshmi	54	M	×	ˇ	×	×	22.0	120/80	124	76	68	16	10	0.90	0.04	0.38	55
74	Ramkumar	48	M	ˇ	ˇ	×	×	26.5	140/70	142	102	42	12	12	0.88	0.06	0.30	55
75	Palanisamy	65	F	ˇ	ˇ	×	×	27.0	120/70	182	92	36	16	10	0.78	0.08	0.32	50
76	Selvamary	66	M	×	×	×	×	20.5	120/80	164	96	52	8	8	0.36	0.10	0.40	60
77	Sundaram	40	F	×	×	×	ˇ	23.5	130/76	128	84	46	8	6	0.46	0.16	0.54	55
78	Kanagavalli	82	M	×	×	ˇ	×	23.0	120/80	163	118	55	7	7	0.76	0.20	0.60	60
79	Swetha	40	F	×	×	×	×	24.5	142/80	121	102	60	6	12	0.92	0.16	0.80	60
80	Manikandan	62	M	×	×	×	ˇ	26.7	126/76	163	129	42	10	14	0.88	0.10	0.80	58
81	Devendran	65	M	×	×	×	ˇ	19.0	110/70	129	79	59	14	18	0.59	0.06	0.30	55
82	Senthilkumar	60	M	ˇ	×	×	×	28.5	120/80	198	149	56	28	22	0.47	0.06	0.48	55
83	Padmavathy	45	F	ˇ	×	×	×	29.0	120/70	147	129	52	16	14	0.79	0.06	0.30	60
84	Sridar	72	M	×	×	×	ˇ	32.5	120/80	156	92	48	14	14	0.78	0.08	0.34	60
85	Saminathan	68	M	×	×	ˇ	×	28.0	132/82	163	101	44	12	12	0.97	0.08	0.50	55
86	Kalairani	40	F	×	×	×	×	24.5	130/70	136	96	58	8	10	0.85	0.06	0.58	60
87	Vadivel	65	M	×	×	×	ˇ	20.5	120/72	176	92	42	6	8	0.36	0.08	0.64	55
88	anthonyammal	50	F	×	×	×	ˇ	21.5	112/70	131	91	63	7	9	0.76	0.10	0.28	60
89	Ramanan	55	M	ˇ	×	×	×	22.0	130/80	152	99	55	11	10	0.42	0.06	0.40	55
90	Devan	40	M	ˇ	×	×	×	24.0	118/70	142	82	48	12	13	0.72	0.11	0.60	50
91	Chinnathai	43	F	×	×	×	ˇ	23.5	130/80	198	149	32	15	17	0.88	0.04	0.30	60
92	Gangadharan	70	M	×	×	ˇ	×	22.5	120/76	169	119	39	19	17	0.39	0.10	0.32	55
93	Janaki	50	F	×	×	×	×	24.0	128/72	138	72	49	22	17	0.72	0.16	0.60	60
94	Egambaram	65	M	×	×	×	ˇ	26.0	110/70	151	107	54	12	14	0.84	0.06	0.26	55
95	Muniyan	45	M	×	×	×	ˇ	19.0	120/80	127	72	65	3	16	0.62	0.06	0.24	45
96	Murugammal	46	F	ˇ	×	×	×	18.5	140/90	163	163	103	42	20	18	0.06	0.26	56
97	Gowrisankar	48	M	ˇ	×	×	×	27.5	120/86	178	142	44	10	12	0.36	0.08	0.09	57
98	Saraswathi	56	F	×	×	×	ˇ	26.0	120/70	165	132	46	18	13	0.38	0.07	0.06	58
99	Samundeswari	65	F	ˇ	×	×	×	23.5	130/80	178	112	54	12	14	0.78	0.08	0.09	56
100	Jeeva	70	M	ˇ	×	×	×	27.5	112/70	163	132	65	18	12	0.46	0.06	0.28	60

ETHICAL COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE, KILPAUK,
CHENNAI- 10.
Venue: PANAGAL HALL, KMC
Dt: 01.02.2011

CHAIRPERSON
Prof. Dr.V.KANAGASABAI, MD.,
Dean
Govt. Kilpauk Medical College, Chennai-10

Sub: Ethical Committee project work - approved – regarding.

Ref: Lr.No.3944/Audit/E1/09 Dt. 30.11.2010

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With above reference, the Institutional Ethical committee meeting for the following students was conducted at our Institution on 01.02.2011.

S.NO.	Name	Topic
1.	Dr.Navin Kumar, MS(Ortho), PG., Govt. Royapettah Hospital, Chennai.	1.To Identify a Safe Zone to approach proximal Humerus 2.To study Anatomical relations of Axillary nerve, its course & its Variations
2.	Dr.T.Satheesh Kumar, D.Ortho., PG., Govt. Royapettah Hospital, Chennai	Heriditary Multiple Exostosis
3.	Dr.J. Jeya Shambavi, MD(Pathology), PG., Govt. Kilpauk Medical College, Chennai-10	Clinicopathological Histomorphological and Immunohistochemical Study of Neuroendocrine Tumors of GIT
4.	Dr.L. R. Saranya. MD., (Paed.)PG., Govt. Kilpauk Medical College, Chennai-10	Cord Blood Zinc Level in Term-Small for Gestational Age Neonates
5.	Dr.A.Satheesh Kumar, MS(ENT), PG., Kilpauk Medical College, Chennai	Study on Cases of Chronic Suppurative Otitis Media in Tubo Tympanic Type Due to Sinusitis as Focal Sepsis
6.	R.Prathiban,(Msc.,Physiology), PG., Student, The TN. Dr.MGR Medical University,Chennai-32	Prevalence of Cardiac Dysautonomia in Type I Diabetes mellitus
7.	B. Manikandan, (Msc., Physiology), PG., Student, The TN Dr.M.G.R. Medical University, Chennai-32.	A Comparative Study of Left Ventricular Structure and Function in Obese and Non Obese Subjects
8.	G. Selvakumar, (MSc., Physiology), PG., Student, The TN Dr.M.G.R. Medical University, Chennai-32.	A Study of the Intraocular Pressure In Patients with Diabetic Normotensive, Diabetic Hypertensive and Normal Subjects

9.	R. Ragulji, (Msc.,Physiology), PG., The TN Dr.MGR Medical University, Chennai-32.	A Study of Pulmonary function in insulin dependent diabetes mellitus
10.	V.M. Jenila Veny,(MscPhysiology), PG. The TN Dr.MGR Medical University, Chennai-32	Cardiovascular Autonomic Dysfunction in Chronic Kidney Disease
11.	Dr.G. Lakshmi, MD(O&G), PG., Govt. Kilpauk Medical College,Chennai-10	A Study of Association of Thyroid Disorders in Abnormal Uterine Bleeding
12.	Dr.R. Harini, MD(O&G), PG., Kilpauk Medical College, Chennai	Single Dose Antibacterial treatment for Asymptomatic Bacteriuria in Pregnancy
13.	Dr.E.Geetha, MD(O&G), PG., Govt. Kilpauk Medical College, Chennai-10	A Study of the incidence course of Pregnancy and Pregnancy outcome in Obstetric Cholestasis and to evaluate the efficiency of UDCA in relieving the Symptoms and Improving the Perinatal outcome in these Patients
14.	Dr.S. Nithya, MD(O&G), PG., Govt. Kilpauk Medical College, Chennai-10	Prospective Study of Prevalence of diabetes Mellitus, Thyroid Dysfunction and Hyperprolactinemia in Recurrent Pregnancy loss
15.	Dr.Mohideen Fathima, MD(O&G), PG., Govt. Kilpauk Medical College, Chennai-10	A Study of evaluation of multi system changes in Gestational hypertension / severe pre-eclamptic/eclampasia patients
16.	Dr.M.Padma Priya, MD(O&G), PG., Kilpauk Medical College, Chennai	Dyslipidemia as a Predictor of PIH
17.	Mrs.G. Savitha, (Msc.,Medical Bio Chemistry), TN Dr.M.G.R.Medical University, Chennai-32.	Association of subclinical hypothyroidism in metabolic syndrome patients
18.	Dr.K. Bharadhwaj, MD(G.M.), PG., Kilpauk Medical College, Ch-10	A Study on Peripheral Vascular Disease in Type 2 Diabetes Mellitus
19.	Dr.B.Priya, MD(G.M.), PG	Study of Serum Bilirubin Concentration in Established Coronary Artery Disease
20.	Dr.R.Hema, MD(G.M.), PG.,	Study of Troponin I level in Supraventricular Tachycardia in Non Cad Patients
21.	Dr.P.Manoj Kumar, MD(G.M.), PG., Kilpauk Medical College, Ch-10	A Study on Pulmonary Functions in Type 2 Diabetes Mellitus
22.	Dr.M.Dhanasekar, MD(G.M.), PG.,	Prognostic Risk Stratification of Acute Coronary Syndrome – Role of Highly Sencitive – Reactive Protien
23.	Dr.N. Karthik, MD(G.M.), PG., Govt.Kilpauk Medical College, Chennai-10	A Study of Comparison of QT Dispersion in Acute Myocardial Infraction Between Early Reperfusion and Late Reperfusion Therapy

24.	Dr.H. Anuradha, MD(G.M.), PG., Kilpauk Medical College, Ch-10	A Study of Stress Hyperglycemia in Moderate Degree Burns
25	Dr. V. Nandakumar, MD(G.M.), PG.,	A Prospective Study of Clinical Profile of Emphysematous Pyelonephritis in Type Two Diabetes Mellitus
26.	Dr.S.Sasikumar, MS(G.S.), PG., Govt. Royapettah Hospital, Chennai	A Study of Unusual Presentations of Appendicitis.
27.	Dr.S.R.Padmanabhan, MS(GS), PG., Govt. Royapettah Hospital, Chennai	A Comparative Study Between Autologous Platelet Rich Plasma and Saline Dressing for Diabetic Ulcer
28.	Dr.C.Rose, Scientist-G and Head, Biotechnology, Central Leather Institute, Chennai.	Wound healing efficacy of the chitosan – containing collagenous biomaterial. on burn wound
29.	E.K. Lavanya,B.Tech, Biotechnology, PG., Prathyusha Institute of Technology and Management, Tiruvallur.	Isolation and Characterization of Bacterial Pathogens from Eye Infection

We are glad to inform you that at the Ethical Committee meeting, the documents were discussed and the above short term projects are Ethically approved.

4/2/11
CHAIRPERSON
. DEAN
Govt. Kilpauk Medical College.
Chennai-10.

To: The Individuals